SURGERY, GYNECOLOGY AND OBSTETRICS

AN INTERNATIONAL MAGAZINE, PUBLISHED MONTHLY

VOLUME LVII JULY, 1933 NUMBER 1

KIDNEY PELVES

NORMAL VARIATIONS IN THEIR SHAPE AND FLOW WITH POSSIBLE PATHOLOGICAL SIGNIFICANCE

D. K. ROSE, M.D., F.A.C.S., ST. LOUIS, MISSOURI
Department of Surgery, Washington University Medical School and Barnes Hospital

WILLIAM G. HAMM, M.D., F.A.C.S., ST. LOUIS, MISSOURI
Resident Surgeon, Barnes Hospital

SHERWOOD MOORE, M.D., ST. LOUIS, MISSOURI
Department of Radiology, Washington University Medical School

HUGH M. WILSON, M.D., ST. LOUIS, MISSOURI
Department of Radiology, Washington University Medical School

EVERY urologist is familiar with the variations in shape, size, and location of kidney pelves. Six years ago it occurred to us that, from the standpoint of hydrodynamics, this variation might be a factor in inviting pathological changes such as pyelonephritis—pyogenic or tuberculous—stone formation, nephralgia, and hæmaturia. It has long been recognized that a completely duplicated kidney pelvis and ureter, though a congenital malformation, may serve an individual perfectly for a lifetime. But it is also well known that in such kidneys drainage is frequently unsatisfactory, predisposing to pathological change. With this in mind we undertook a study of less complete abnormalities, that is, pelves which, while classified as normal might, in the process of emptying, permit either constant or temporary stasis of small amounts of urine, in all or in certain portions of the kidney pelvis, and thus predispose the organ to any of the pathological changes in which stasis is a recognized etiological factor. Such a pelvis we have termed "dysuric."

There has been a satisfactory clinical application of these ideas since their inception. Three hundred and eighty five pyelograms, together with the histories of the cases have been analyzed and this has led to the following conclusions:

A "non-dysuric" kidney pelvis is one in which the drainage system of the kidney is symmetrically placed throughout the renal tissue and furnishes free flow of urine through all its parts; from minor to major calyces, to pelvis, to ureter, because of the following: The capacity interrelationship of these parts one with another; the sufficiency of the angle of junction of one part with another; and the freedom from peristaltic interference of any unit with that of another. In such kidneys there will be neither permanent stasis nor transient "crowding" of urine in any one or more of the principal drainage "units"; major calyces, minor calyces, pelvis, or ureter.

It follows that a kidney deficient in any of the requirements for a "non-dysuric" pelvis is either actively or potentially "dysuric." An actively "dysuric" pelvis is one in which

the flow is imperfect in the absence of a secondary stasis factor. A potentially "dysuric" kidney pelvis is one which may require change in position, an increased fluid intake, alteration in the blood supply, infection, change in intrapelvic pressure (secondary to some outside interference with the drainage system), or trauma, to institute the "dysfunction." It is our belief that pelves showing one or more physiologically obstructive emptying defects can cause obscure symptoms, objectively as in idiopathic hæmaturia, or subjectively alone as in a nephralgic kidney. Or they can be a factor in pathological change such as infection (simple or tuberculous) or in calculus formation.

The term "stasis" is employed here to designate two types, one acute or complete retention, and the other partial, incomplete, or intermittent retention. The former produces a thinning in the musculature of the obstructed organ while the latter primarily induces compensation by hyperplasia of the muscle. Depending upon the degree and the type of resistance in play this increased force of the muscular contraction traumatizes causing pain or hæmorrhage or both and continues and exacerbates an infection. The actual stasis following the stage of muscular decompensation produces a relative anæsthesia, the result of the long continued pressure in a thinning musculature. Therefore, incomplete stasis, in its inception and early phases, induces an hypertrophy of the musculature and, because of its early resistance to retention, additional trauma with actually less retained urine results. In the later stages there is greater retention of urine with less muscular resistance but with an infection superimposed.

We believed that a classification which would enable us to analyze the drainage facilities of the individual kidney would aid in discovering stasis of urine in all or in some portion of the kidney pelvis or ureter. If stasis could be discovered a missing etiological factor in certain kidney diseases would be known. Our classification begins with complete duplication of the pelvis and ureter and progresses through types and degrees "of dysuric" pelves to those of the "non-dysuric" type.

In a normal individual each kidney is responsible for the formation and output of, suggestively at least, one-half the total amount of urine. This urine is transmitted to the bladder by a dilatable neuromuscular system which is moveable in all its component parts from fat enclosed intrarenal calyces to pelvis and ureter. Peristaltic contraction forces the fluid from minor to major calyces to pelvis, to ureter. Within the kidney this contraction is made possible by the freedom of motion afforded by the fatty tissue which cushions the calyces and intrarenal pelvis.

In order to evaluate the drainage requirements of each portion of the kidney pelvis, relative to the drainage facilities present, we divided the kidney into units, accepting papillæ (represented pyelographically by minor calyces) as the primary drainage unit. These units (papillæ) average from six to fourteen (occasionally more) in number and furnish an exit for an average of approximately two hundred papillary ducts of the entire kidney. The superior and inferior pole papillæ have one-third to one-half more papillary openings than the lateral as they drain the poles as well as the adjacent lateral pyramids. The pyramids may vary somewhat in length in accordance with the shape of the kidney and placement of the pelvis, but not to the same extent as do the calyces. In other words, the calyces extend to the emptying tips of the pyramids rather than the pyramids reaching to the calyces. The lobulations on the surface of the kidney do not indicate the number of pyramids as we understand that term because there are also interstitial lobules in the columns of Bertini.

Spatzholz states: "The medulla surrounds the renal sinus and is made up of an average of thirty conical masses" which he calls pyramids. The apices of these end in papillæ and project into the renal sinus at the beginning of the calyx. The apices of the pyramids become fused so that each papilla represents two or three pyramids at the center of the kidney and six or more at the upper and lower poles.

The importance of this functional division of the kidney lies in the fact that one can grossly estimate the amount of urine which

Pyelogram 1.

Pyelogram 2.

Pyelogram 3.

Pyelogram 1. Completely bifid pelves and ureters. A. J., female, aged 24 years. In this case the ureteral orifice from the superior calyx entered the bladder above that from the lower pelvis. No history of infection or nephroptosis although there was a history of pyelitis in childhood. Pain was reproduced by overdistention of the superior pelvis with sterile water through a ureteral catheter. This pole had dilated very little due to its small requirement and capacity. Drainage of the lower portion was unusually direct and blocked that of the upper by ureteral contact. Other pyelograms outline the minor calyces of the upper portion which, apparently, are two in number. Resection of the upper pole gave immediate relief. Unfortunately, on the fifth day after operation, a severe secondary hæmorrhage occurred requiring a pedicle clamp with subsequent removal of the remaining portion of the kidney.

Pyelogram 2. Completely bifid pelves and ureters. A. K., female, aged 28 years. Nephralgic right kidney. Pain was reproduced by overdistending the superior calyx which is of a secondary pelvic type with small capacity yet has at least three pyramidal openings, thus having a capacity requirement of at least one-third of the total urinary output of one kidney. Furthermore, when the urine is received by this small, deeply placed, intrarenal storage space it causes greater back pressure pain by reason of further interference with the flow from ureteral contact. Such a pelvis suffers greater stress at times of large fluid intake. This type of stasis (upper pole) causes pain but does not tend to maintain a permanent infection on account of the rapid peristalsis. The lower pelvis might show stasis at times, cause no pain on account of greater elasticity, but permit of sufficient multiplication of organisms to invite pyelitis, etc. There is no record of surgery in this case.

Pyelogram 3. Nephralgic bifid kidney pelvis and ureter, not infected. V. F., female, aged 23 years. Pain was relieved at times by ureteral catheterization, at other times made worse. Patient's typical pain could be reproduced by filling the upper calyx. While distention of the lower calyx caused pain, it did not reproduce the typical pain. Heminephrectomy, upper pole, was done with perfect relief. There was no evidence of scar tissue or aberrant blood vessel at operation. We believe the "dysuric" factor to have been a ureteral interference both by direct contact of one ureteral wall with the other, and by the peristaltic wave of the larger (lower) portion interfering with the emptying of the upper portion. There was no associated nephroptosis.

Fig 1. Completely bifid pelves and ureters. Actively "dysuric" if the ureters in their normal position, offer sufficient interference to peristalsis by contact to cause any degree of stasis. This stasis will occur in that portion having the less perfect drainage system. Potentially "dysuric" to a sensitive degree when any of the described secondary "dysuric" factors coexist. In such kidneys the ureters normally cross twice although occasionally single crossing occurs. Overdistention of the ureters with pyelographic media and ureteral catheter often, on pyelogram, alter the true picture of the ureters.

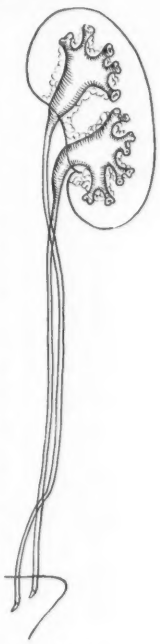


Fig. 1.

each major calyx receives from the number of minors emptying into it and, with this as a basis, estimate the required storage capacity of these receiving calyces and of the pelvis.

We find that no special type of kidney pelvis can arbitrarily be termed "dysuric" from its gross appearance. The drainage system of each individual kidney must be analyzed according to pelvic and calycine capacity, contour, angles of junction of one part with another, and all these must be taken into consideration and one's opinion based upon the possibilities of stasis in any of the drainage

Pyelogram 4.

Pyelogram 5.

Pyelogram 6.

Pyelogram 7.

Pyelogram 4. H. M., female, aged 20 years. Primipara with postpartum pyelitis, right side only. Ureters join midway, dilatation above the crest of the ilium. The "dysuric" factor renders a poor prognosis for eventual sterilization of urine and suggests that a pyelitis of infancy or childhood, leaving a low grade infection, was the etiological factor in this postpartum pyelitis. Pyelogram of left kidney was not obtained. It is important to note here that the drainage of both parts is excellent, at least to the junction of the ureters. The lower portion is dilated more than the upper because it carries the catheter, the upper being filled by reflux. This pyelogram is presented to emphasize the idea that pyelitis of pregnancy may be a recurrence of pyelitis of infancy and that often there is a "dysuric" factor present which renders the prognosis of the pregnancy pyelitis poor from the standpoint of complete disappearance of the organism. A pyelitis of pregnancy which is secondary to an altered function, and which presents no "dysuric" renal factor, congenital or acquired, offers a better prognosis from the standpoint of the ultimate disappearance of all organisms.

Pyelogram 5. E. M., female, aged 15 years. Backache, cystitis (Bacillus coli), appendectomy previously performed. Pyelogram shows unilateral incompletely bifid pelvis and ureters. No infection present. While the left kidney was clear at the time of its catheterization, we feel that it was probably the source of the cystitis and that, even though on the left side, it might have caused the backache and bladder symptoms. The pyelogram demonstrates the point that the right and left pelves in the same individual can be markedly dissimilar.

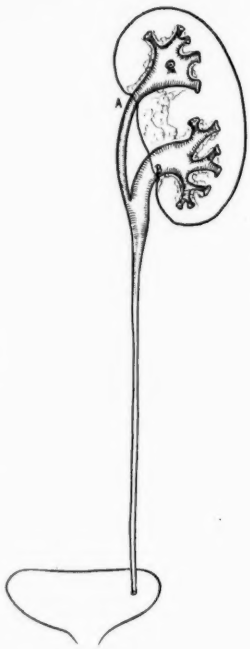


Fig. 2.

Pyelogram 6. R. C., female, aged 23 years. Nephralgia, incompletely bifid pelvis and ureter with the superior calyx of the secondary pelvic type. This, by its large output, small capacity, and angle of junction of its ureter with that of the lower pelvis, has gradually caused the muscle of the lower pelvis to decompensate. The inferior ureterocalycine line is suggestively sharp indicating that the pelvis is deeply placed within the renal sinus. This, in turn, suggests that the lower portion had a small true pelvic and large calycine capacity which would assist the upper portion in its victory over the lower. A heminephrectomy of the lower portion was performed.

Pyelogram 7. M. D., female, aged 52 years. Left nephrolithiasis, cystitis since childhood at present complicated by stone. Analysis shows a sharp inferior ureterocalycine line with the ureteral "Y" definitely visible. The kidney is somewhat dilated by a long standing, low grade pyelonephritis. The opposite kidney pelvis and ureter are normal and present no symptoms. It is suggested that in this case the congenital malformation evidently played a part in the early and continued pyelonephritis which, in association with stasis, contributed to the stone formation.

Fig. 2. Incompletely bifid pelves and ureters. May be actively "dysuric" by virtue of the angle of junction of the ureters, or disproportion between the drainage capacity and requirement of the two portions. Either major division may gain the right of way thus damming up the remaining portion. May be potentially "dysuric" particularly in the upper major calyx should a change in the position of the kidney cause a slight degree of angulation and obstruction at its junction with the inferior major calyx.

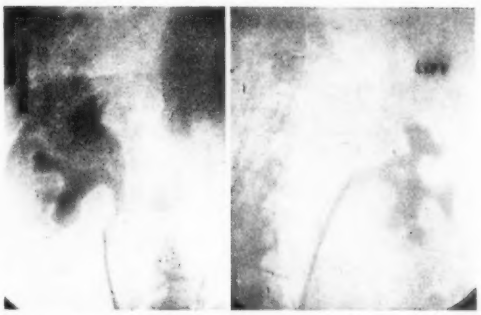
Pyelogram 8. F. L. M., male. Acute pyelonephritis following sphenoidectomy. By an estimate of the minor calyces we feel that the lower portion has a capacity requirement of the inflow of one minor calyx more than the upper portion which is of a definite secondary pelvic type. The upper infundibulum is anatomically and functionally a continuation of the ureter (there is no common pelvis) into which the lower infundibulum enters at an unsatisfactory angle (almost 90 degrees). The flow from the upper blocks the outflow from the lower by its rapid peristaltic flow. Close observation suggests that the lower calyces are thickened and blunted by a spreading of the minor calyces rather than by a pushing up of the papilla. From this analysis we feel that the lower portion is infected. The part which shows stasis in any bifid type of pelvis is determined by minor accessory "dysuric" factors.

Pyelogram 9. J. Y., female. Perinephric abscess, bifid pelvis. While there is no common pelvis present and a large calycine capacity, the distribution of the drainage system to renal tissue is good and the angle of entrance of the two infundibula excellent. The chief "dysuric" point in this bifid pelvis is the large calycine capacity. The kidneys were not infected at the time of ureteral catheterization. Could this relative minor calycine stasis of urine sometimes be a factor in perinephric abscess?

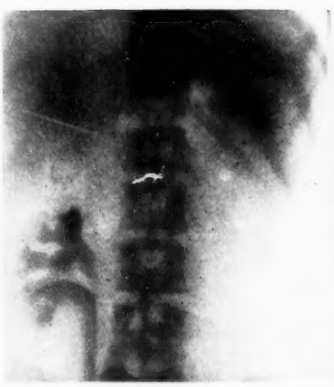
Pyelogram 10. M. M. D., female. Tuberculous kidney, no operation. The chief "dysuric" points are the absence of a common pelvis, large calycine capacity, and the junction of the two divisions. That is, the lower has larger calycine capacity requirement. Early stasis would be likely to occur in the lower portion, chiefly the deeply placed minor calyces, when the upper pole was in the process of emptying. Nearly two-thirds of the kidney's output must use the lower infundibulum. One cannot satisfactorily visualize the junction of the infundibula.

Pyelogram 11. G. L. Pyelitis of pregnancy, gravida-iii, pyelitis associated with first and last pregnancies. Left kidney not infected although definitely "dysuric" in outline. Right kidney shows a typical dilatation of pregnancy. While the left kidney is bizarre, one cannot point to a definite inequality between the upper and lower portions. The fact that the upper portion has the greater capacity requirement and the most direct drainage argues heavily against any pelvic dysfunction. A peristaltic wave beginning above passes directly down the ureter tending to block the lower portion which has, however, sufficient capacity for storage while the upper portion empties. The lateral calyces in the upper portion, if of sufficient output, could block the upper part of that division. We feel that the left side has to do with the original introduction of the organism. If we could reconstruct the mild right hydronephrosis, possibly but not probably, it might present a "dysuric" factor. In a rapidly emptying pelvis such as the left, organisms are recovered with difficulty at times of large fluid intake. This pyelogram is presented to show our inability to diagnose definitely a "dysuric" pelvis from a single pyelogram and to illustrate the possible sources of error in culture or stain of urine from a rapidly flowing pelvic stream.

Fig 3. Bifid type of intrarenal pelvis with no common or true pelvis. Functionally this type is quite similar to that in Figure 2. Anatomically the only difference lies in that here the infundibula (functioning as bifid ureters) of the superior and inferior major calyces join within the renal sinus rather than along the course of the ureters.



Pyelogram 8. Pyelogram 9.



Pyelogram 10.

Pyelogram 11.

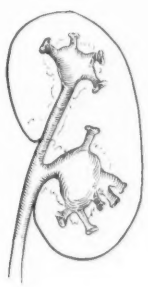
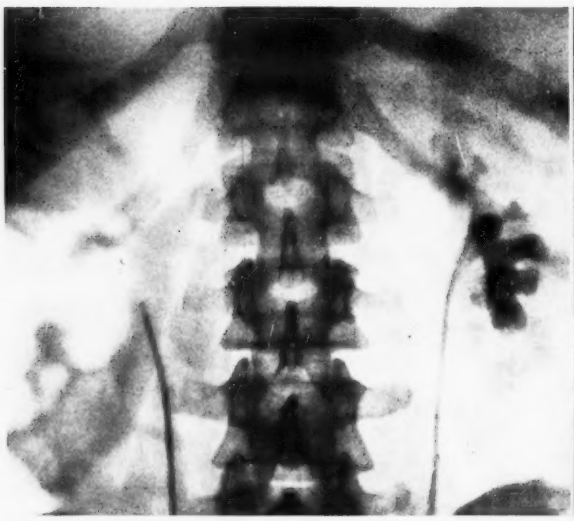


Fig. 3.



Pyelogram 12.

Pyelogram 13.

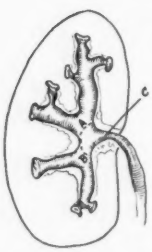


Fig. 4.

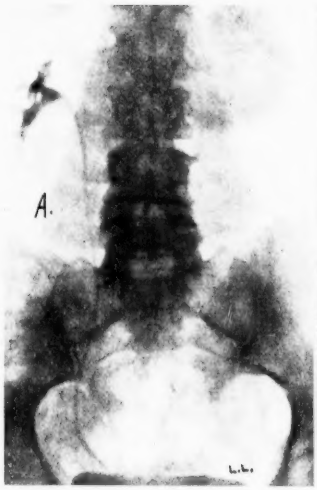
Pyelogram 12. H. B., male. Tuberculosis, left kidney. Large calycine with small common pelvic capacity. The lower portion had a direct outlet in the small common pelvis into which the upper empties through a narrow infundibulum (in which the tip of the ureteral catheter rests). There is some dependency of the inferior calyx which, at the time of nephrectomy showed early pelvic tuberculosis. In such pelves we believe that the parenchymatous tuberculous lesion ruptures into the pelvis which, in turn, is predisposed to secondary involvement depending upon the degree of "dysuria" present. It would be interesting to note that healed renal tuberculosis occurs in "non-dysuric" pelves.

Pyelogram 13. G. G., female. Tuberculous pyonephrosis which shows dilatation of the minor calyces. The kidney pelvis proper has a very small capacity. It is this type of kidney pelvis which can often become infected at several points, that is, a more general intrapelvic spread secondary to a primary parenchymatous lesion. It would be equally susceptible to a regurgitant (bladder) or lymphatic (ureteral) spread of the infection. In contrast to this a true bifid kidney and ureter shows a slow spread to the portion of the better drainage. As this pelvis can be reconstructed to its original type, small pelvic and large minor calycine capacity of lesser degree only than presented here, so also can most dilated pelves be reconstructed, at least mentally, to their approximate original size and outline. Often, one is able to determine that a marked dysfunction was a primary factor in the kidney damage. In this case due to a lack of a common pelvis, each minor calyx served as its own reservoir while the others emptied. The attempt of the kidney to excrete organisms without damage to itself failed due to stasis and pressure trauma within these units, thus allowing the organism to invade the pelvic mucosa. In this manner a vicious circle of "dysuric" factors was instituted.

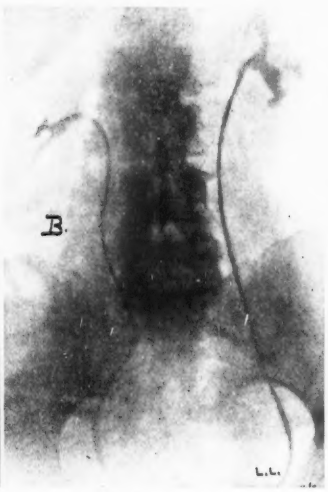
Fig. 4. Small true pelvis with consequent large calycine capacity. This "dysuric" formation occurs so often in association with other factors such as a bifid type of intrarenal pelvis (Fig. 3) that it is difficult to establish it as a separate "dysuric" entity. Its importance lies in that if a perfect balance does not exist between calyces of rather large though insufficient capacity, and one of them, by virtue of its greater requirement becomes blocked in any degree by other portions having better drainage facilities, one will eventually show some stasis.

units, before a kidney can be designated as "non-dysuric" or "dysuric."

The most important single result of "dysuria" in any portion of the drainage system of the kidney is stasis. Stasis invites infection by allowing time for organisms to multiply. It produces nerve and vascular symptoms by pressure. Stasis of urine may occur in a portion of the pelvis as a result of the commandeering of its outlet by the superior drainage facilities of another portion, or it may occur in the entire pelvis because of insufficient storage capacity. In either instance we have muscular thickening (compensation) and eventually thinning or dilatation (decompensation). A dilating portion of the kidney pelvis first occupies the circumscribing fat area and later encroaches on the



Pyelogram 14.



Pyelogram 15.

Pyelogram 16.

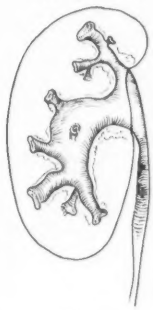


Fig. 5.

Pyelograms 14 and 15. L. L. Female. Pyelonephritis, right. Pyelogrom 14 was taken with patient in the recumbent position, 15 with patient in the erect position. The dependent, large capacity, calyx and the inferior ureterocalycine line are definitely altered on a very slight degree of ptosis. The superior (secondary pelvic type) calyx shows continued direct emptying with the altered position. This type is rare and constitutes a minor degree of dysfunction but, in our experience, can exhibit a degree of lower calycine stasis. It is usually seen with other "dysuric" factors notably small pelvis with large calycine capacity.

Pyelogram 16. M. N., female. Nephralgia and pyelonephritis (Bacillus coli) left. Dependent inferior major calyx with a capacity demand of 50 per cent of the kidney's output. This calyx is of a suggestively secondary pelvic type (much more frequently found in the superior calyx) and empties through a common pelvis of small capacity. For these reasons stasis could occur and, with a large fluid intake (not necessarily with the addition of other secondary "dysuric" factors), could cause overdistention with pain and pelvic trauma. Such a dependent calyx associated with small true pelvic capacity would predispose to a chronic pyelonephritis in our opinion.

Fig. 5. High placed sinus renalis with consequent dependency of major capacity portion of the renal pelvis. The chief "dysuric" factor here is the lower major calycine dependency which being deeply placed within the kidney causes a sharp inferior ureterocalycine line. The upper calyces have better drainage facilities and gain the right of way over the larger dependent calyx in which stasis may occur.

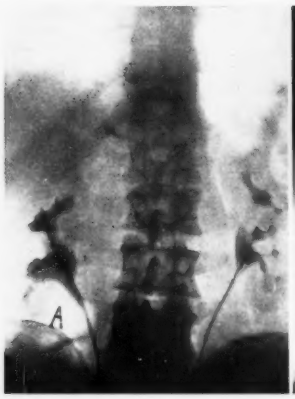
renal tissue by pressure. When this occurs the pelvis loses its sensitivity to back pressure through a physiological pressure anæsthesia. Because of this, in retrograde filling, greater pressure is required to develop renal pain on the involved side and such pelves are often seen to be overdistended with pyelographic fluid. As decompensation progresses, vascularity of mucosa and muscularis diminishes.

Necessarily, the more renal tissue that calyces of small capacity must drain, the more rapid must be the flow of urine thus requiring more frequent and stronger peristaltic waves. A pelvis which at first glance appears to be bizarre may be normal in its mechanics, whereas one which is apparently "non-dysuric" may, on analysis, prove to be "dysuric" in a marked degree. For example, even a spider leg pelvis may be "non-dysuric" if all its angles and capacities are distributed to insure even and unobstructed flow of urine. A small pelvis tends to "overcrowd" and produce calycine back pressure. A large square pelvis, on the other hand, with consequent small calycine capacity, empties slowly, and this may be a factor in producing stasis. An extrarenal pelvis offers less resistance to back pressure than one which is intrarenal. Therefore, if it is not infected, upon dilatation, pain or bleeding is less likely to occur than it would in a deeply placed intrarenal pelvis of similar capacity but with less elasticity.

Pyelogram 17.

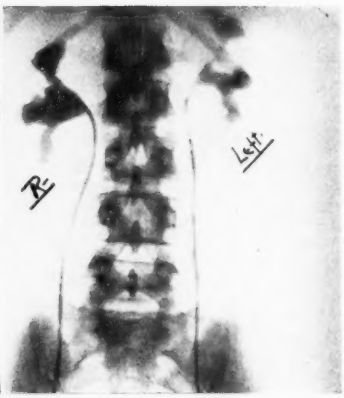
Pyelogram 18.

Pyelogram 19.



Pyelogram 20.

Pyelogram 21.

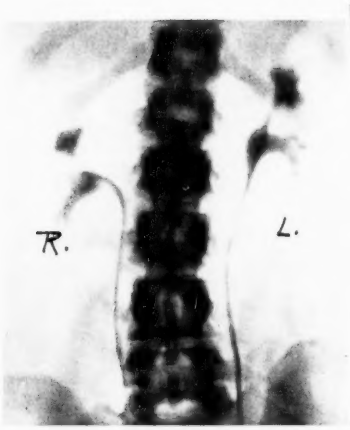


Pyelogram 22.

Pyelogram 17. K. S., female, aged 50 years. Pyelonephritis, left; nephralgia, left. Shows dilatation of the superior major calyx due to lack of a common pelvis of sufficient capacity. In the competition for an emptying right of way, the capacity demand or calycine requirement and angle of entrance of the infundibula into the pelvis favored the lower calyces with consequent dilatation of the upper portion of the pyelonephritis being secondary to the stasis.

Pyelograms 18 and 19. G. Q., male, nephralgic left kidney, pyelonephritis, left. The "dysuric" upper portion is brought out by the two pyelograms. The "dysuria" is due to a large capacity demand of the upper portion with a small outlet through the true pelvis. It is not functionally a direct continuation of the ureter. The upper portion, functionally, has two ureteropelvic junctions to clear instead of one. The upper enters into a cavity already filled with urine and occupied with its own peristaltic duties. These particular pyelograms were made by filling, in Pyelogram 18, rapidly to the point of pain and, in Pyelogram 19, very slowly allowing extracatheter flow to the lower major calyx which represents the common or true pelvis. They are also shown to present a picture often seen in "emptying films." Pyelogram 19 represents what is normally the first pyelographic finding. The catheter is then withdrawn and in 7 or 8 minutes Pyelogram 18 is taken. The lower portion has now emptied leaving the upper full. In this case the condition is partly due to the "dysuric" factors and partly to a temporary paralysis of the smooth muscle produced by the acute overdistention. In similar pelves, also, when the tip of the catheter terminates in the lower calyx, the pyelographic media may pass to the bladder before filling of the upper major calyx takes place. All of which illustrates the dysfunction of the superior major calyx.

Pyelograms 20 and 21. T. G., male. Pyelonephritis (Bacillus coli) left, normal right kidney. On the left we feel that the drainage facilities of the superior calyx are inadequate due to the smallness and length of its infundibulum as well as to the fact that it enters a pelvis serving the remainder of the kidney. Functionally, the superior calyx has two ureteropelvic junctions. The right superior



Pyelogram 23.

Pyelogram 25.

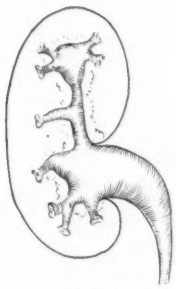


Fig. 6.

calyx has a large infundibulum and is not infected but is potentially "dysuric." The slight kinks in the right superior infundibulum, Pyelogram 20, and the left superior infundibulum, Pyelogram 21, are due to overdistention causing approximation of the superior calyx and its common pelvis. Such kinks could occur with a secondary "dysuric" factor.

Pyelogram 22. A. McG., female, aged 25 years. Primipara. Pyelitis of pregnancy (streptococcus). Right pelvic dilatation, not infected, left pelvis infected. From a "dysuric" standpoint this is quite similar to Pyelograms 20 and 21. The superior left calyx suffers stasis with varying degrees of increase in intracalycine pressure.

Pyelogram 23. M. R., female. Pyelonephritis, bilateral (Bacillus coli). Nephroptosis with pain, right. The "dysuric" point is bilateral and similar to that in Pyelograms 20, 21, and 22. Emptying film in this type of pelvis, taken with patient erect, frequently shows nephroptosis with retention of pyelographic media in the superior major calyx.

Pyelogram 24. W. L., male. Left pyelonephritis (Bacillus coli). Is quite similar to the other pyelograms shown to illustrate this type of "dysuria" except that the superior infundibulum is broader and has a better angle of entrance. It has, however, a minor calyx of considerable output representing a type which, in some instances, could impede the flow down a narrow infundibulum leading from a superior calyx of large capacity demand, through a common pelvis to the ureteropelvic junction.

Pyelogram 25. M. G., female. Tuberculosis of the left kidney. Shows two varieties of long (inadequate) superior infundibula leading from superior calyces of secondary pelvic type and of very considerable capacity demand. Left kidney removed and showed most extensive tuberculous pelvic involvement of the superior portion. The right kidney is potentially "dysuric." Bacillus coli was present in the bladder urine one year after operation. The remaining right side has not been catheterized but is probably infected with Bacillus coli only.

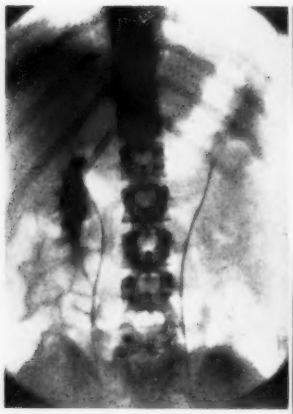
Pyelogram 26. W. E., male. Right kidney normal, "non-dysuric." Shows kink of the superior infundibulum and upper ureter of quite similar degree due to a one degree ptosis and overdistention. The width of the entrance to the superior calyx into the pelvis is unusually broad as is the infundibulum itself.

Pyelogram 24.

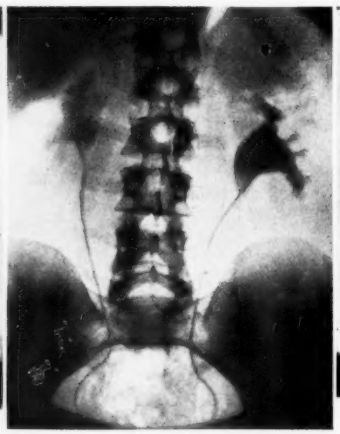
Pyelogram 26.

Fig. 6. Low placed renal sinus with consequent long superior infundibulum with secondary pelvic type of superior major calyx. The infundibulum enters into the common pelvis at or approaching a right angle and may have minor calyces emptying into it, often at right angles also. These two points suggest peristaltic interference along the course and at the emptying point of the calyx. Furthermore, while the long upper infundibulum enters the common pelvis within the renal sinus, its point of entrance is not quite as mobile as though it joined the ureter directly as in Figure 3. On change of position of the kidney this point is subject to kink causing nephralgia and trauma by overdistention of the deeply placed, secondary pelvic type of superior calyx. This type is commonly met with and, as all others, is frequently associated with other "dysuric" factors of pathological importance. The superior ureterocalycine line is of importance in recognizing this type.

Whether a pelvis, either actively or potentially "dysuric," is of interest from a pathological point of view, is determined by analyzing the pyelogram for one or more of the following drainage interferences. Usually there is one major "dysuric" factor which



Pyelogram 27.



Pyelogram 28.

Pyelogram 29.

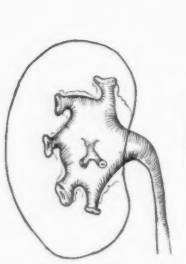


Fig. 7.

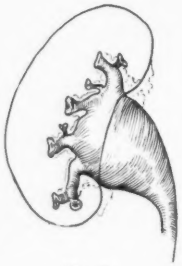


Fig. 8.

Pyelogram 27. H. E., female. Pyelonephritis with intermittent nephralgia. Intrarenal pelvis with large true pelvic but small calycine capacity. In our experience this type is rare. The nephralgia was apparently secondary to the infection. The slow flow through such a pelvis gives time for multiplication of organisms. An indwelling ureteral catheter is successful in such pelves in that a common drainage basin is emptied thereby. In many instances a ureteral catheter blocks one portion of a pelvis while draining the remainder.

Pyelogram 28. R. J., male. Represents overdistention with pyelographic media of an extrarenal, small calycine, large, true pelvic capacity type. Pyelonephritis, no nephralgia. This is the type represented by Figure 8, having in addition a secondary pelvic type of superior calyx of small capacity on a short and relatively narrow infundibulum which, however, does not seem to exhibit a sufficient degree of "dysuria" to be of importance.

Pyelogram 29. J. O., female, aged 6 years. Acute pyelonephritis. Recovered bacteriologically in a short time. It is easy to feel that there is some stasis in such a pelvis although it is entirely "non-dysuric." An unusually large or virulent infection coming through the blood stream or an ascending infection might find favorable reception for at least a longer time than a pelvis with more rapid flow.

Figs. 7 and 8. Large true or common pelvis with consequent small calycine capacity. The large pelvis results in slow emptying particularly at the time of small output. This alone, in some instances, constitutes a "dysuric" factor exactly to the degree that occurs in an early hydronephrosis whether or not it is infected. Figure 7 represents a large, deeply placed *intrarenal* pelvis with consequent sharp inferior uterocalycine line. It is more susceptible to secondary "dysuric" factors and also is less distensible without symptoms upon dilatation than is the corresponding extrarenal pelvis. One seldom has severe pain in this type as the peripelvic fat allows of considerable distention. Figure 8, the large *extrarenal* pelvis with small calycine capacity, overdistends so readily that the pyelogram usually suggests an early hydronephrosis.

possibly would not be important were it not for some additional minor interference with the flow. The points to be considered are:

1. Placement of the kidney within the body (degree of ptosis or rotation).

2. Shape and size of the kidney (from long and thin to short and thick).

3. Opening of the hilus (high, middle, low, anterior, or posterior).

4. Undesirable superior or inferior ureterocalycine line (formed by the line from the superior minor calyx over the pelvis to the ureter, and by the marginal line from the inferior minor calyx to the lower surface of the pelvis to the ureter, respectively). Such lines give indication of the relationship of pelvis to renal hilus and substance as well as of size, shape, and position of pelvis, and of the influence of these upon the ureteropelvic junction. The inferior ureterocalycine line shows particularly the depth of the pelvis within the renal substance.

5. The number, size, and distribution of the minor calyces and their relationship to the

major calyces (indicating the capacity requirement of the latter).

6. Size and angle of entrance of minor into major calyces and of major calyces into pelvis, and of pelvis into ureter. (Artificial dilatation incident to pyelography may alter these angles and sizes). Pelvis dilatability is of great importance in estimating stasis possibilities.

7. Ratio of capacity, shape, and location of pelvis to those of the calyces, that is the total capacity of major plus minor calyces, and the interdependent capacity requirement and placement of each of these units.

The association of two or more of the above "dysuric" factors, even when each is of very moderate degree, often produces marked dysfunction of the pelvis. Likewise, large fluid intake, outside pressure, change in position of the kidney or alteration in its blood supply, may institute symptoms when only a moderate degree of drainage deficiency is present.

On account of the co-existence of one or more "dysuric" points in a pelvis a diagnostic classification is presented below in order to stress the major, individual "dysuric" factor. The secondary or contributing "dysuric" factors are discussed in the accompanying pyelograms. The latter are intended to emphasize the association of diverse "dysuric" factors. In these pyelograms the diagnosis is mentioned but no type of "dysuric" pelvis is, in our opinion, specific for any one pathological change.

FIGURE 1

Bifid pelves and ureters (complete reduplication).

Pyelogram 1 Pyelogram 2 Pyelogram 3

FIGURE 2

Bifid pelves with incomplete reduplication of the ureter. The ureters draining an upper and lower major calyx which, in capacity and relation to renal substance may be markedly dissimilar to each other.

Pyelogram 4 Pyelogram 5
Pyelogram 6 Pyelogram 7

FIGURE 3

Bifid pelves with the infundibula of the superior and inferior major calyces serving as the ureters as in Figure 2 but joining within the renal sinus and with no common pelvis or only a very small one. *Functionally* this is quite similar to incomplete reduplication of the ureters.

Pyelogram 8 Pyelogram 9
Pyelogram 10 Pyelogram 11

FIGURE 4

A small kidney pelvis with large calycine capacity.

Pyelogram 12 Pyelogram 13

FIGURE 5

Renal sinus entering high with consequent relatively large dependent calycine capacity. (A very rare occurrence.)

Pyelogram 14 Pyelogram 15 Pyelogram 16

FIGURE 6

Renal sinus entering at a low level with consequent relatively large superior calycine capacity. (Occurring most frequently and in association with many other "dysuric" factors.)

Pyelogram 17 Pyelogram 18 Pyelogram 19
Pyelogram 20 Pyelogram 21
Pyelogram 22 Pyelogram 23
Pyelogram 24 Pyelogram 25
Pyelogram 26

FIGURE 7 FIGURE 8

Pelves of large capacity but with relatively small calycine capacity, Figure 7 intrarenal, Figure 8 extrarenal in type. This type of pelvis we consider potentially "dysuric" in that stasis occurs much more readily than in a small pelvic type. The uninfected extrarenal type is more readily distensible without resultant pain or bleeding than the intrarenal.

Pyelogram 27 Pyelogram 28 Pyelogram 29

RELATIONSHIP OF "DYSURIC" PELVES TO RENAL PATHOLOGY

An analysis of the history and pyelogram on 385 cases shows the following significant figures:

In 79 cases with normal kidneys but in which pyelographic study was made to rule out kidney or lower urinary tract pathology, only 17 showed a "dysuric" type of kidney pelvis. In these 17 examples the abnormality was, without exception, of very slight degree.

Forty-one cases of renal calculus were studied, 33 having a "dysuric" type of pelvis, 4 "non-dysuric" and 4 undetermined. There was associated pelvic infection in 14 of the "dysuric" pelves and in 1 of the "non-dysuric" type.

Of 33 nephralgic kidneys without other demonstrable cause for the pain, only 2 were "non-dysuric" the remaining 31 showing varying degrees of "dysuric" pelves.

In nephroptosis with resultant symptoms the 43 cases showed 29 "dysuric" and 14 "non-dysuric," while the 10 cases which showed an associated infection were all of the "dysuric" type.

There were only 11 cases of renal tuberculosis in our series and 9 of these had a "dysuric" type of pelvis while 1 of the remaining 2 showed so much destruction of kidney tissue that the type of pelvis could not be determined. The remaining case was "non-dysuric."

Of 10 examples of idiopathic or essential hæmaturia, 7 had a "dysuric" type of pelvis and 3 were "non-dysuric."

PYELONEPHRITIS

Of 135 cases of pyelonephritis studied, 27 could have been complicated by pregnancy. The latter cases have been considered separately and the following discussion concerns only pyelonephritis without other obvious cause of urinary pelvic stasis. We value greatly the many splendid and valuable papers discussing the mode of infection and the routes by which the organism gains entrance into the kidney pelvis. Our consideration is based solely upon the idea that, under similar conditions, a "non-dysuric" pelvis will clear itself of infection more rapidly and in a larger number of instances than will a "dysuric" pelvis. The damming up of urine in any part of the pelvis permits a constant growth of organisms from which the remainder of the urinary tract may be reinfected. The degree of dysfunction present within the pelvis and ureter, all other factors being equal, determines the age in life at which kidney symptoms manifest themselves. For example, an infant with atresia of the ureteral orifice develops infection early in life while a mild type of "dysuric" pelvis may develop an essential hæmaturia late in life.

Undoubtedly a large percentage of cases of pyelitis in infancy recover clinically. In order to determine whether or not they also recover bacteriologically, it is necessary to search a specimen of urine which has been incubated within the patient's bladder for from 3 to 6 hours. It is in the type of case in which the patient recovers clinically but not bacteriologically that "dysuric" pelves are most important in the prognosis of pyelonephritis. Pelves potentially "dysuric," that is only actively "dysuric" upon change of position or with the introduction of some other secondary factor as previously mentioned, often show great improvement with bed rest.

Besides the influence of "dysuric" pelves we believe that continuation of a pyelonephritis is often due to an interchange of organisms between bladder and pelvis. In the early and acute stages, this occurs via the blood stream but in the subacute and chronic stages it may take place via the peri-ureteral lymphatics or by direct regurgitation. As the bladder incubates organisms in larger numbers, frequent and continued bladder irrigations will often clear up the pyelonephritis when the pelvis is "non-dysuric." A pyelonephritis in a markedly "dysuric" pelvis, while benefited in some instances, does not offer an equal prognosis from bladder treatment alone. In certain "dysuric" types an *occasional* pelvic lavage may still be advised to advantage in that less altered ureteral or calycine physiology may seriously affect the drainage within such a pelvis.

PYELONEPHRITIS OF PREGNANCY

We feel that "dysuric" kidney pelves should be added to the other etiological factors frequently discussed in this connection. Their importance lies in the fact that such an imperfect drainage system lends itself more readily to infection even when only very slight back pressure dilatation is present. When a bilateral pyelogram shows a dilated right side to be infected we are much more likely to find the left infected also if it be "dysuric" and not infected if "non-dysuric." We have found the occasional left sided infection in pyelonephritis of pregnancy, in the absence of dilatation, to be associated with a "dysuric" left kidney pelvis and explain it on this basis in some instances.

As in simple pyelonephritis the prognosis is affected by the degree of "dysuria" present. It also seems probable that, in such pelves, a low grade infection could have persisted from infancy or childhood to exacerbate in pregnancy.

NEPHRALGIA

A nephralgic kidney, lacking discoverable complicating factors, can be explained by the existence of types of actively "dysuric" kid-

ney pelves. In these there is "crowding" of urine either in the entire pelvis or a portion thereof. Of the nephralgic kidneys in our study, the type of actively "dysuric" kidney pelvis encountered most frequently proved to be a very small true pelvis in which the storage capacity was made up of the infundibula and calyces. The pain in this type of "dysuric" kidney pelvis appears to be influenced particularly by large intake of fluid.

The potentially nephralgic kidney most frequently encountered in our analysis was one in which the emptying system of the superior calyx was altered by even a slight change of position resulting in some degree of interference with its emptying. In 2 instances of completely duplicated pelves and ureters with pain due to interference with ureteral drainage, relief was obtained by resection of the "dysuric" half of the kidney. In both instances we had been able to reproduce the pain complained of by overdistention through a ureteral catheter placed in that part which proved to be the "dysuric" portion. In nephralgic kidneys we believe that the painful period is before dilatation occurs, that is at the time of muscular hyperplasia developed to overcome the slight obstruction. The greater the visible dilatation the more pressure is required, upon retrograde filling, to reproduce pain or bleeding (in the absence of infection). This is due to the dilated, weakened muscle and associated pressure anæsthesia of the nerve terminals. Intrarenal pelves, though surrounded by fat and, therefore, capable of considerable distention, offer greater resistance than extrarenal pelves and those situated far out on the hilus.

IDIOPATHIC (ESSENTIAL) HÆMATURIA

From the standpoint of a "dysuric" pelvis alone we believe that a hæmaturia can result from identical factors as those set forth under nephralgia. Of the series of 10 cases of idiopathic hæmaturia 7 showed easily recognizable types of "dysuric" pelves. The analysis resolves itself into generalized or localized pressure causing rupture of minute or small superficial vessels. Before the period of dilatation a low grade inflammatory change may be a secondary cause. This low grade infection may be primary or secondary to a mild pelvic and papillary change due to the transient, intracalycine "crowding" of urine which takes place. To account for an essential hæmaturia by pressure alone, however, a very definite "dysuria," either active or potential, must be found, that is, one in which a definite "crowding" of urine occurs within a resistant or inelastic pelvic or calycine wall.

CALCULUS

Stasis is generally accepted as one of the frequent etiological contributory factors in the formation of kidney calculus. We concur in this view. We are also of the opinion that calculus formation can be traceable to the stasis accompanying a "dysuric" pelvis and that the stone forms in that portion of the "dysuric" pelvis in which the greatest "crowding" of urine occurs. In a very high percentage of cases in which stone was found early in life, it occurred in a "dysuric" pelvis. Of the 41 cases studied 33 were in "dysuric" pelves.

Throughout the analysis of these kidney pelves it is insistently recurring that familial kidney disease, infection and stone particularly, does occur and that it is probably associated with a hereditary tendency to "dysuric" types of kidney pelves. Why should not the shape of the kidney pelvis associated with the general shape of the kidney, in turn associated with body habitus, be found as frequently constant from a familial standpoint as, for example, the shape of the face, nose, etc.?

TUBERCULOSIS

Of 11 tuberculous kidneys 9 were "dysuric." The deep seated pelvis of small capacity with large calycine capacity appeared to be particularly prone to a generalized pelvic tuberculosis. A "dysuric" type of superior calyx became involved frequently without pyelographic evidence of tuberculosis in the remainder of the kidney. Analysis of the 9 "dysuric" pelves definitely suggests that lack of free drainage in all or in part of the kidney leads to a pelvic type of tuberculosis with secondary parenchymatous spread through that part of the kidney tissue drained by the

most "dysuric" portions of the pelvis. It seemed in every instance that the pelvic tuberculosis was secondary to a primary and older parenchymatous lesion.

NEPHROPTOSIS

We have all been impressed with the fact that a kidney lying in the skeletal pelvis may not be nephralgic whereas one with uncomplicated slight motility may. In our 43 cases of nephroptosis 29 were "dysuric." We were not able to make an analysis of statistical value because it was impossible to eliminate all other factors which might have been associated with the nephroptosis in the production of symptoms. We did find definite evidence that, no other factor considered, the potentially "dysuric" kidney pelvis became actively so upon change of position. Most frequently this occurred in conjunction with a change in the angulation of the ureteropelvic junction, and is shown by the type of inferior ureterocalycine line or the nature of the junction of the long superior calyx with the superior ureterocalycine line. The more acute the angle between the superior calyx and the pelvis the more prone is the superior infundibulum to kink upon change of renal position. When there is a change in the angulation at the ureteropelvic junction, there is "crowding" of urine or back pressure in the entire pelvis. When it occurs at the junction of the superior calyx and pelvis the "crowding" is only in the superior portion of the pelvis. Therefore, a long narrow kidney with renal sinus set low, from a "dysuric" standpoint alone, is apt to become nephralgic upon a moderate degree of nephroptosis.

Another type likely to become nephralgic upon change of position is the deep seated, intrarenal pelvis, indicated by a sharp, curving, inferior ureterocalycine line. Drainage deficiency or lack of elasticity or other contributory factors, such as blood vessel or ureteral contact, back pressure, etc., need be present to a lesser degree in "dysuric" pelves in order to cause pain in association with a change in renal position.

CONCLUSIONS

From an analysis of 385 pyelograms and case histories, evidence is presented that kidney pelves, generally accepted as normal, can be so shaped and so related to the parenchyma as to interfere with the free flow of urine either in the entire pelvis or in a portion thereof. Such pelves are termed "dysuric."

The analysis of the pyelograms on the basis of the "dysuric" factors described gives *functional individuality* to all kidney pelves and ureters.

The final importance of such pelves lies in the fact that they permit urinary stasis in all or in part of the pelvis and that this stasis can be and is of importance in the formation of calculi, the inciting and continuation of infection (simple or tuberculous), and in the etiology of idiopathic hæmaturia and nephralgia. Application of the facts set forth here are of value in defining the etiology, instituting and continuing the treatment, and determining the prognosis in renal pathology.

PROTECTION OF PERITONEUM AGAINST INFECTION[1]

BERNHARD STEINBERG, M.D., TOLEDO, OHIO
Laboratories and Department of Medical Research, Toledo Hospital

HARRY GOLDBLATT, M.D., CLEVELAND, OHIO
Institute of Pathology, Western Reserve University

THE work here described presents a method and a material for protection of the peritoneum against varied bacterial contamination. In dogs, this protection is achieved in 12 to 48 hours by a single intraperitoneal injection.

By a method of vaccination previously published (3, 6), little or no protection was afforded by a single injection. A total period of 10 to 12 days and four daily injections of heat killed colon bacilli suspended in physiological saline were required for a maximum protection. Subsequently, it was found (4) that the protection was most probably due to a local peritoneal polymorphonuclear response and a rapid phagocytosis of the organisms. Other experiments (2) had demonstrated that after intraperitoneal introduction of bacteria suspended in physiological saline, the bacteria rapidly pass from the peritoneal cavity into lymph and blood. Consequently, because of this rapid disappearance of the saline suspension of bacteria from the peritoneum, the local cellular response was insignificant and no protection was obtained from a single injection of the bacterial suspension. It necessitated several intraperitoneal injections for a sufficient bacterial retention and peritoneal irritation in order to evoke the exudation of enough polymorphonuclears to combat an infection. It was also observed (2) that bacteria suspended in a gum tragacanth solution, when injected intraperitoneally, were retained in the peritoneal cavity.

The following experiments were carried out in order to determine whether heat killed bacteria (our strain colon bacillus No. 300), suspended in gum tragacanth, when injected intraperitoneally, would protect animals against various forms of bacterial peritoneal soiling. The injection of the suspension of dead organisms in gum tragacanth solution will be referred to in the following discussion as peritoneal vaccination.

EXPERIMENTAL PROTECTION

The experiments were divided into several groups. In the first experiments, the time was varied between the peritoneal vaccination and the infection of the peritoneum with living organisms, to test the degree of protection, but the quantity of the protective substance was kept constant. In the second group of experiments, the type of infection was varied but the time factor and the quantity of the infecting substance were kept constant. In the third group, the number of killed bacteria (which constituted one of the two ingredients of the protective substance) was varied. The other ingredient, 1 per cent of gum tragacanth in physiological saline solution, remained constant. The type and amount of infecting substance were kept constant. In the fourth group, the total quantity of both ingredients of the vaccine was increased but the type of infecting substance and the time interval between vaccination and infection were kept constant. The fifth group of experiments constituted controls. Each part of the protective substance was injected separately, to test the protective capacity of each ingredient. All the other factors (time interval between vaccination and infection, quantity of material injected, type of peritoneal infection) remained constant.

Group 1. Thirty-four dogs were injected intraperitoneally with 50 cubic centimeters of a 1 per cent solution of gum tragacanth in physiological saline in which were suspended heat killed Bacilli coli (our culture No. 300, heated at 80 degrees C. for 10 minutes). The bacterial suspension contained about 200 million organisms in 1 cubic centimeter. At varying intervals (12, 24, 48, and 72 hours) following this protective intraperitoneal injection, the peritoneum of the 34 animals was infected by an intraperitoneal injection of 40 cubic centimeters of 2.5 per cent gum tragacanth in physiological saline in which were

[1]This work was aided in part by a grant from the Committee on Scientific Research of the American Medical Association to (S) and from the Littauer Foundation, New York, to (G).

TABLE I.—RESULTS IN GROUP I

Interval in hours between vaccination and peritoneal infection	No. dogs used	No. dogs dead	Percentage survival*
12	5	3	40
24	10	4	60
48	10	2	80
72	9	2	77
Not protected	26	26	0

*In all of the tables, although the number of animals used is not very large, percentages of survival are given only for the purpose of easier comparison of the results.

TABLE II.—RESULTS IN GROUP II

Character of peritonitis produced	Interval in hours between vaccination and peritoneal infection	No. dogs used	No. dogs dead	Percentage of survival
Intraperitoneal injection of 40 c.cm. of 2.5 per cent gum tragacanth with 200 million bacteria per c.cm.	48	15	3	80
Not protected		8	8	0
Appendix ligated at base, perforation made at tip, fæcal contents expressed and smeared manually over peritoneum; perforation left open	48	6	2	66
Not protected		2	2	0

suspended about 200 million living Bacilli coli per cubic centimeter. It was found (Table I) that the 48 hour and 72 hour intervals between the vaccination and the peritoneal infection gave the highest percentage of survivals. When the infecting injection was made 12 hours following the intraperitoneal protective injection only 40 per cent of the animals survived. Twenty-six control dogs were not vaccinated but were given the same intraperitoneal injection of living Bacilli coli in gum tragacanth as the 34 vaccinated animals. All of the control dogs died.

Group 2. Twenty-one dogs were injected intraperitoneally with 50 cubic centimeters of a suspension of heat killed Bacilli coli in 1 per cent solution of gum tragacanth in physiological saline. The bacterial suspension contained about 200 million organisms in 1 cubic centimeter. Forty-eight hours after the protective injection 15 of the animals were infected with an intraperitoneal injection of living organisms (Bacillus pyocyaneous, Streptococcus

TABLE III.—RESULTS IN GROUP III

No. heat killed Bacilli coli suspended per c.cm. in 1 per cent gum tragacanth	No. dogs used	No. dogs dead	Percentage of survival
200,000,000	10	2	80
1,000,000	6	2	66
500,000	6	4	33
100,000	6	4	33

fæcalis, and Bacillus welchii isolated from a case of human peritonitis) suspended in 2.5 per cent gum tragacanth in physiological saline. The bacterial suspension contained about 200 million living organisms more or less evenly divided among the three bacterial species. Of the 15 vaccinated animals, 12 survived.

Eight unvaccinated control dogs were given the same intraperitoneal infecting injection. All died (Table II).

In the 6 remaining vaccinated dogs, peritonitis was induced by ligation of the appendix at the base, perforation of the tip and manual spread of the fæces over the visceral and parietal peritoneum. The appendiceal perforation was allowed to remain open. In addition to the 6 vaccinated animals, 2 normal dogs were similarly treated by ligating and perforating the appendix. Four of the 6 vaccinated animals survived. The two control dogs died.

Group 3. Twenty-eight dogs were injected intraperitoneally with 50 cubic centimeters of 1 per cent gum tragacanth in physiological saline in which were suspended varying numbers of heat killed Bacilli coli. In one group of 10 animals, the protective substance contained about 200 million Bacilli coli per cubic centimeter (these 10 animals constituted part of Group 1). In 3 other groups of 6 animals each, the protective substance contained about 1 million, 500,000 and 100,000 organisms per cubic centimeter, respectively. Forty-eight hours following the protective injection an intraperitoneal injection of 40 cubic centimeters of a suspension of living Bacilli coli in 2.5 per cent gum tragacanth was given. The animals vaccinated with the largest number of organisms showed the greatest percentage of survivals. The group vaccinated with the smallest number of organisms had the smallest percentage of survivals (Table III).

TABLE IV.—RESULTS IN GROUP IV

Interval in hours between vaccination and peritoneal infection	No. dogs used	No. dogs dead	Percentage of survival
18	6	0	100
24	6	0	100
Control dogs not protected	6	6	0

TABLE V.—RESULTS IN GROUP V

Type of material used for protection	No. dogs used	No. dogs dead	Percentage of survival
1 per cent gum tragacanth in physiological saline	5	5	0
A suspension of heat killed Bacilli coli in physiological saline	5	5	0

Group 4. Twelve dogs received a protective injection of 100 cubic centimeters of a suspension of heat killed Bacilli coli in 1 per cent gum tragacanth in physiological saline. The suspension contained about 200 million organisms per cubic centimeter. Eighteen hours after the protective injection, 6 animals were given an intraperitoneal injection of 40 cubic centimeters of a suspension of living Bacilli coli in 1.25 per cent gum tragacanth in physiological saline. Twenty-four hours after the protective injection, the 6 remaining vaccinated animals also received the same amount and type of intraperitoneal injection of living Bacilli coli in gum tragacanth solution. All of the vaccinated animals survived.

Six control dogs that were not vaccinated received the same intraperitoneal injection of living Bacilli coli in gum tragacanth as the vaccinated animals. All of the control animals died.

Group 5. Five dogs were injected intraperitoneally with 50 cubic centimeters of 1 per cent gum tragacanth in physiological saline. Five other dogs were injected with 50 cubic centimeters of a saline suspension of heat killed Bacilli coli, containing 200 million organisms per cubic centimeter. Forty-eight hours following these intraperitoneal injections the peritoneum of the 10 dogs was infected by the intraperitoneal injection of 40 cubic centimeters of a suspension of living Bacilli coli in 2.5 per cent gum tragacanth. The 10 dogs died (Table V).

Examination of animals. All of the dogs that survived the peritoneal infection were eventually killed and examined. In addition, 10 dogs were killed which had received only 50 cubic centimeters of the protective material. One dog from every group was killed every week. A small amount of exudate persisted in some dogs for a month. Of the 10 vaccinated animals that were not given an infecting intraperitoneal injection, none had peritoneal adhesions. Of the groups of vaccinated animals that also received the infecting intraperitoneal injection, a few of the animals showed slight adhesion of a loop or two of bowel to the abdominal wall. Gross and microscopic examination of the viscera failed to show any striking abnormalities.

MECHANISM OF PROTECTION

The reactions within the peritoneal cavity were investigated by hourly withdrawal of the peritoneal exudate. This was done by piercing the abdominal wall with a glass capillary pipette. Cell counts were made by means of the standard white and red blood cell pipettes and counting chamber. Bacteria were counted by the dilution and plating method (1). The type of cell, the differential counts, and the degree of phagocytosis were determined from stained films (Wright's stain and methylene blue).

The following protocol will serve as an illustration of what happens in the peritoneal cavity following the intraperitoneal injection of heat killed Bacilli coli in 1 per cent gum tragacanth. This series of events was studied in 16 animals and was similar in all.

A dog was given intraperitoneally 50 cubic centimeters of a 1 per cent solution of gum tragacanth in physiological saline in which were suspended about 200 million heat killed Bacilli coli per cubic centimeter. The number of white cells in the peritoneal exudate was counted at hourly intervals following the injection. Up to the fourth hour there was a gradual increase in the number of polymorphonuclear leucocytes. After that the number vacillated but continued generally to rise (Chart 1). The reason for this fall and rise of polymorphonuclears will become apparent in the later experiments. In 10 hours, the white cell count in the peritoneal exudate rose to

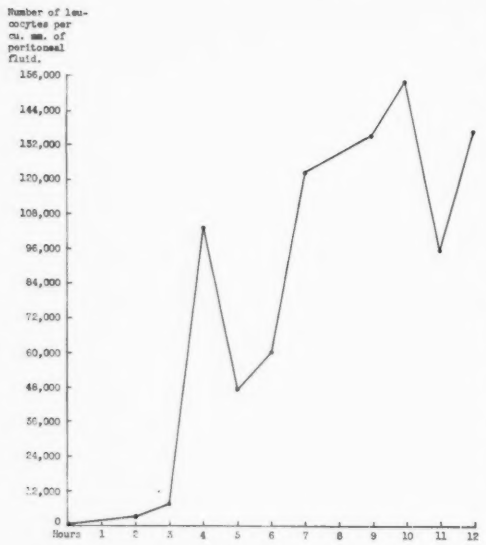


Chart 1. Hourly white cell counts of the peritoneal exudate (per cu. mm.) in a dog which received intraperitoneally 50 cubic centimeters of a 1 per cent gum tragacanth in physiological saline in which were suspended about 200 million heat killed Bacilli coli per cubic centimeter.

153,000 per cubic millimeter. In 24 hours, the count was 240,000 and in 72 hours 460,200. The white cells persisted in appreciable numbers in the peritoneal cavity for 26 days. At the end of the first week, there were 52,200 cells, at the end of 16 days 124,000 and on the twenty-sixth day 31,600 cells per cubic millimeter of peritoneal exudate. For the first 48 hours the cells were predominantly polymorphonuclear in type. In 72 hours and from then on, there was an appreciable increase in the mononuclear and a decrease in the polymorphonuclear type.

The following protocols will serve as an illustration of what happens in the peritoneal cavity when a peritoneally vaccinated animal is given an intraperitoneal injection of living Bacilli coli suspended in gum tragacanth.

Two dogs were vaccinated by the intraperitoneal injection of 50 cubic centimeters of 1 per cent gum tragacanth in physiological saline in which were suspended about 200 million heat killed Bacilli coli per cubic centimeter. Forty-eight and 72 hours later, respectively, the peritoneum was infected by the injection of 40 cubic centimeters of a suspension of living Bacilli coli in 2.5 per cent gum tragacanth. At the end of 1 hour, peritoneal *cell counts* of the two animals showed a marked decline in the number of cells compared with the number present in the peritoneal cavity prior to the injection of the suspension of living organisms (from 266,000 and 537,500 to 13,500 and 8,500, respectively). At the end of the second and third hours, the cell counts had increased greatly and from then on there was a fall and rise in the number of cells (Chart 2). The *bacterial count* of the peritoneal exudate showed a great decrease in the number of viable bacteria in 1 hour following the infection of the peritoneum (Table VI). The fall and rise of the number of cells corresponded more or less with the fall and rise of the number of bacteria. The examination of stained films of peritoneal exudate disclosed at the end of the first hour practically complete phagocytosis of the bacteria, with very few organisms free in the fluid of the exudate. However, at the end of the third hour, of the many polymorphonuclears which were present only a few (about 5 per cent) contained phagocytosed bacteria, and there were many degenerated cells.

From the correlation of the peritoneal cell counts, the bacterial counts and examination of stained films, it is assumed that the fall in the number of the polymorphonuclear leucocytes is due to two factors: (a) degeneration of the cells, and (b) the passage of cells with phagocytosed bacteria from the peritoneal cavity into the lymphatics and blood vessels. The subsequent rise in the number of cells is accounted for by the passage of new polymorphonuclears in the exudate from the vessels into the peritoneal cavity. The presence of young forms and bacteria-free cells in the stained films are evidence in favor of this assumption.

The type of cell which was phagocytic for bacteria was the polymorphonuclear. The mononuclear type of cell (monocyte, clasmatocyte) was present in small numbers at the onset of infection and did not increase until the living bacteria had practically disappeared from the peritoneal cavity.

TABLE VI.—BACTERIA COUNTS

Counts of living bacteria in the peritoneal exudate of two vaccinated dogs and one unvaccinated dog after peritoneal injection with a suspension of living Bacillus coli in gum tragacanth solution.*

Hours following peritoneal infection	Bacteria per c.cm. of peritoneal exudate in:		
	Control unvaccinated dog	Dog vaccinated 48 hrs. before infection of peritoneum	Dog vaccinated 72 hrs. before infection of peritoneum
1	27,360,000	500	156,000
2	33,000,000	2,000	5,000
3	14,000,000	2,500	12,000
4	6,740,000	5,500	16,200
5	880,000	7,000	12,500
6	240,000	7,500	8,000
7	560,000	5,500	6,500
8	14,000,000	1,500	2,000
9	10,300,000	200	7,000
10	4,160,000	1,000	6,000

*The number of living bacteria in the suspension used for the infection of the peritoneum was in every case about 200,000,000 per c.cm.

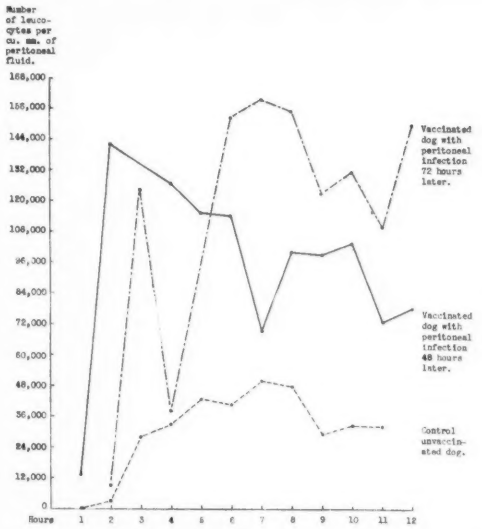


Chart 2. Hourly white cell counts of the peritoneal exudates (per cu. mm.) in dogs which received intraperitoneally 50 cubic centimeters of 1 per cent gum tragacanth in physiological saline in which were suspended about 200 million heat killed Bacilli coli per cubic centimeter. Forty-eight hours and 72 hours later, each dog respectively was given intraperitoneally 40 cubic centimeters of 2.5 per cent gum tragacanth in physiological saline in which were suspended about 200 million living Bacilli coli per cubic centimeter. The peritoneal cell counts of an unvaccinated control dog with a similar type of peritoneal infection is included to show the relative number of cells in protected and unprotected dogs. Count before injection in vaccinated dog with peritoneal infection, 266,000, 48 hours later; 537,500, 72 hours later.

CLINICAL APPLICATION

In 100 patients, from 12 to 48 hours prior to surgical operation, an intraperitoneal injection, consisting of a suspension of Bacilli coli No. 300 in 1 per cent gum tragacanth in physiological saline, was given. The injection consisted of 30 cubic centimeters of this suspension which contained about 200,000,000 organisms per cubic centimeter. The point of injection was in the midline, a little below the umbilicus. The urinary bladder was emptied by the patient prior to the injection. The needle used was No. 15 gauge, 2 inches long, to insure penetration of the abdominal wall.

One-half hour prior to the intraperitoneal injection, one-sixth to one-quarter grain of morphine sulphate was given and repeated at 4 hour intervals for 16 hours. The reactions (abdominal pain and slight elevation of temperature) are those of a peritoneal irritation and the former can be controlled with morphine. The protective substance was administered in cases in which there was danger of peritoneal soiling: resection of intestine (especially large bowel), intestinal anastomosis, "interval" appendectomy, chronic pelvic conditions with adhesions, requiring removal of pelvic organs. A definite contra-indication to the use of this method is an already developed and clinically demonstrable general peritonitis. A detailed report of this phase of the work will be given at a later date. Of the 100 patients treated to date none developed acute peritonitis.

As an interesting illustration the following case is cited: A patient with an annular carcinoma of the colon was protected 18 hours prior to the operation. During the operative procedure the bowel was torn and fæces escaped into the peritoneal cavity. The patient did not develop peritonitis.

DEDUCTIONS

The factor responsible for the protection of the animals with the killed Bacillus coli gum tragacanth mixture is apparently predomi-

nantly phagocytosis by polymorphonuclear leucocytes. The introduction of the protective substance and its retention in the peritoneal cavity evoke the exudation of a large number of polymorphonuclears which are available for phagocytic action at the time of the infection. This phenomenon has been designated by one of us (5) as "hyperleukocytic preimmunity."

This protection must be regarded as nonspecific since the protective material was effective not only against the Bacillus coli but also against the Bacillus pyocyaneous, Streptococcus fæcalis, Bacillus welchii, and other organisms found in fæces. After the nonspecific character of the protection was determined, Bacillus coli gum tragacanth peritonitis was used throughout the experiments as the test for the existence of protection because it is an easily controlled standard procedure. The particular organism and strain (Bacillus coli No. 300) was used as protective substance because it happened to be excellent for the production of hyperleucocytosis in the peritoneal cavity.

There is an apparently direct quantitative relationship between the amount of the protective substance used, and the percentage of survival of the animals. Larger amounts of the substance resulted in a greater percentage of surviving animals. Neither one of the components of the protective material singly could protect against a fatal outcome when the infecting injection was made within 72 hours.

CONCLUSIONS

1. A material and a method are presented for the protection of the peritoneum against infection. In dogs, a single intraperitoneal injection is effective within 12 hours, against peritoneal infection with Bacilli coli and other intestinal bacteria which are often found associated with acute peritonitis.

2. The material acts by evoking a polymorphonuclear hyperleucocytosis and a consequent rapid phagocytosis of living organisms.

3. This method of protection has been used clinically in 100 cases of possible peritoneal soiling at operation. Although the number of cases is too small for a positive determination of the protective effect, yet it is noteworthy that none of these patients developed peritonitis.

REFERENCES

1. Karsner, H. T., Brittingham, H. H., and Richardson, M. L. J. Med. Research, 1923, xliv, 83.
2. Steinberg, B., and Goldblatt, H. Arch. Int. Med., 1927, xxxix, 449.
3. Idem. Arch. Int. Med., 1928, lxii, 415.
4. Steinberg, B., and Snyder, D. A. Arch. Path., 1929 viii, 419.
5. Steinberg, B. Proc. Soc. Exper. Biol. & Med., 1931, xxix, 18.
6. Idem. Arch. Surg., 1932, xxiv, 308.

EPITHELIOMATA OF THE LOWER RECTUM AND ANUS

THEODORE S. RAIFORD, M.D., NEW YORK
From the Department of Surgery and the Laboratory of Surgical Pathology, The Presbyterian Hospital, Columbia University

ONE is surprised at the infrequent reference in modern medical literature to the group of ano-rectal epitheliomata for, although rare, these tumors comprise a well known pathological entity. Textbooks of rectal surgery allude to them as members of the pernicious group of rectal neoplasms but detailed descriptions of their clinical and pathological characteristics are negligible. It is true that only a small percentage of all gastro-intestinal neoplasms are of this nature. Pack places their incidence at 3 to 4 per cent of all rectal cancer and the few other investigators who have ventured to refer to their frequency have agreed that the incidence is less than 5 per cent. Among the 352 proved malignancies of the rectum in the files of the Presbyterian Hospital, only 10, or 2.8 per cent, were of squamous cell nature.

Feeling that this group of tumors should occupy a more prominent place in the description of gastro-intestinal neoplasms, the author has attempted an analysis of these 10 cases from the standpoints of clinical features, pathology, prognosis, and treatment. The results of this study form the basis for the following paper.

HISTORICAL

Epitheliomata of the anus and rectum have undoubtedly long been known as pathological lesions of the terminal bowel but it is questionable if the earlier pathologists and surgeons realized the malignant nature of the lesion and treated it as more than a simple ulcer or polyp. Reviewing the sparse literature on the subject one comes across few descriptions of the tumor until the latter half of the nineteenth century. Much more common, however, were the chronic ulcers and fissures which persistently refused to heal in spite of local treatment and in which the patients frequently succumbed to cachectic disease. Bushe records one of the earliest malignant epitheliomata of the anus which, because of the inefficiency of treatment at that time, terminated fatally. Allingham, in 1879, commented upon the rarity of the lesion but it is quite probable that he mistook many of the neoplasms for benign rodent or lupoid ulcers. Several of the latter which he described caused death from the late effects of the disease, a fact which must have signified metastases and extention. In spite of Lisfranc's earlier work on resection of the rectum, Allingham regarded operative procedures as hopeless and deforming and preferred to treat the condition primarily along palliative lines. Van Buren was one of the first to give a lucid description of the growth and, commenting upon its similarity to squamous cell cancer of the lip, advised excision as a hopeful measure in early cases. The subsequent experience of surgeons at large has contributed little to the subject in general and many regard the entity as an insidious and hopeless condition in the majority of cases. The increasing use of radium and X-ray therapy has brightened the outlook in epitheliomata and some investigators are exceedingly optimistic regarding the results after interstitial radiation.

OCCURRENCE

The number of cases in this series is so small that conclusive deductions cannot be drawn as to their distribution between the sexes and races and the ages at which they occur. The following statements are, therefore, referable only to the cases observed in this clinic and should not be regarded as generalities.

The white race was more susceptible to the condition, the ratio of whites and blacks affected being four to one. It should be recalled, however, that white people come under hospital observation more commonly than do negroes. Only 2 of the 10 patients were males. This is a surprising and interesting finding in view of the general prevalence of gastro-intestinal cancer among males but this

too, cannot be considered a constant feature of the disease unless borne out by a large number of cases. Unfortunately, the cases reported in the literature are so few that such a positive deduction would be erratic. The age distribution corresponded roughly to that of carcinoma elsewhere in the body, the average age being 48.7 years.

ETIOLOGICAL FACTORS

Little can be authoritatively said in regard to the etiology of any malignant growth. As irritation has come to be regarded as a contributing factor in cancer of the oral cavity, however, so has a similar influence been recognized in epitheliomata of the anus. Fissures, fistulas and chronic ulcers are among the common lesions from which anal malignancy is thought to develop. Many pathologists claim to have observed true cancer developing in the bases of such lesions and in many other incidences the two conditions have been reported coincidental. In still other cases the tumors have been said to have developed in the sudoriferous or sebaceous glands, cicatrices, moles or psoriatic patches. Proof of the relationship between such so called precancerous lesions and fully developed malignancy, however, is still lacking and must be considered as a matter of conjecture. Overexposure to X-rays has been considered the definite stimulating factor in many cases of skin cancer, and it is therefore logical to assume that epitheliomata of the anus can be produced in the same way. Such was thought to be the agent in one of the cases in this series and will be discussed more fully in a later section of the paper.

Gant has attempted to trace the development of the anal epithelioma through its various stages. According to his hypothesis, the forerunner of the tumor or the precancerous lesion is the small papillary excrescence or the benign ulcer. This in its process of growth forms the nodular, indurating tumor which in turn gives rise to the large indolent ulcer, the typical epitheliomatous manifestation. Correlation with the microscopical findings is not in complete accord with this theory and shows that these various gross forms signify different histological tumor types.

In résumé, one can assume that since irritative lesions frequently precede and accompany epitheliomata, they may play an important rôle in the development of the latter. To designate which is cause and which is effect is more difficult and to state dogmatically that such lesions are the etiological agents of cancer would be extremely didactic.

CLINICAL ASPECTS

Clinical recognition of the lesion is facilitated by its accessibility although diagnosis of the malignant nature is particularly difficult in the early stages.

Pain is the most constant and depressing feature of the condition and may be of two types. Tumors producing infiltrating subcutaneous masses cause a dull pain which is aching, boring, or throbbing in character. Sedatives provide some relief but the patient is constantly aware of a heavy sensation in the lower pelvis which bowel evacuation fails to relieve. If on the other hand the surface of the tumor is ulcerated the frequent irritation of passing fæcal material or the cleansing process following a bowel movement produces an intense burning pain comparable to that of fissure. Itching not infrequently precedes the onset of actual pain by weeks or even months and the irritation and excoriation produced by the patient's attempts to relieve himself are no doubt contributory to the course of the disease.

Bleeding is a common symptom and is characteristic of low rectal growths. It occurs when the tumor is ulcerated. Fresh and bright red in color, it is usually recognized by the patient as streak of blood on the stool or as spots upon the undergarments. Copious hæmorrhage or tarry stools rarely occur. In the majority of cases the growth is located outside the anus or near enough to enable the patient to recognize an unusual mass or ulcer by palpation. On many occasions this may be the first warning of any pathology.

Symptoms of obstruction can be produced if the marginal growth forms a cicatrix about the anal aperture. More rarely low intrarectal growths plug the anus from above by a ball-valve effect. In either event, the obstruction is characterized more frequently by

tenesmus and a sensation of heaviness in the pelvis than by distention and meteorism.

Constitutional symptoms appear late after the disease has become well established. Loss of weight may be more or less marked but secondary anæmia and cachexia are less pronounced than in the case of large bowel malignancies.

The physical manifestations are usually sufficiently characteristic to make the diagnosis. The general appearance of the patient does not always show the devastating effects of malignant disease if the condition is in its early stage. Emaciation and debility are rarely marked unless the growth is of long duration and has undergone extensive metastases.

The appearance of the lesion itself is usually characteristic but varies somewhat with the type of growth and the degree of malignancy. The small papillary excrescence is perhaps the earliest and most benign form. It resembles a condyloma or venereal wart and the differentiation is sometimes difficult. At other times the tumor appears as a small peri-anal ulcer no more than a few millimeters across, with an excavated center and a hard indurated base. This latter forms the extensive indolent ulcer similar to certain forms of epitheliomata elsewhere on the body if allowed to grow unmolested. This ulcer has a hard, granulating base with raised and overhanging edges. The area bleeds easily to touch and exudes a foul smelling seropurulent fluid.

The less common manifestation of the lesion is a nodular warty growth which usually begins near the anal margin, later extending out into the peri-anal tissues producing an irregular deformity of the skin. Pressure is painful, accentuating the dull pain from which the patient is a constant sufferer. If the tumor originates inside the anal orifice or extends deep into the tissues of the ischiorectal fossa, it may not be apparent to external examination. In this event digital palpation usually reveals the mass as a definite tumor or a sense of resistance outside the lumen, especially when counter pressure is applied to the perineum with the other hand.

Laboratory findings show little of significance and, indeed, these are not essential to diagnosis. A moderate secondary anæmia is the rule. If the tumor is ulcerated and secondarily infected a slight leucocytosis is to be expected. X-ray findings have little to offer due to the superficial location of the growth. Biopsy is, of course, the most valuable laboratory procedure and is the only certain means of differentiating a malignant tumor from a benign lesion.

DIAGNOSIS

The diagnosis of epitheliomata by means of biopsy is relatively easy but on the basis of clinical observation alone the condition must be differentiated from several other lesions.

Non-specific ulcers lack the hard cartilaginous base characteristic of the malignant epithelioma and tend to regress under local treatment. *Tuberculosis* not infrequently forms cutaneous ulcers or may even produce a tumor or stricture low in the rectal canal. It may be a source of diagnostic confusion but is softer and is usually coincident to tuberculosis elsewhere in the body. Certain forms of *eczema* are not infrequently confused with the precancerous, scaly keratosis, especially when irritated. *Fissures* and *fistulas* because of their insidious manner of growth are a source of common error in diagnosis. Differentiation is all the more difficult since the relation between the two is still a moot question. *Venereal warts* and *condylomata* are grossly similar to some types of epitheliomata but thorough laboratory study should rule these out.

Other types of tumor growth about the anus often necessitate biopsy for diagnosis. *Carcinomata* arising from the lower rectum and extending away from the bowel lumen infiltrate the subcutaneous tissue and form palpable lumps beneath the peri-anal skin. *Epitheliomata* of the perineal skin may extend to and involve the anus secondarily. *Melanomata* are not grossly unlike true squamous cell epitheliomata except when the characteristic bluish-black color is evident. Among the rarer conditions encountered are peri-anal *lymphangiomata, endometriomata* of the recto-vaginal septum in females, *cysts and tumors* of the postanal gut, *anomalies* of the *procto-*

deum and *coccygeal vestiges*. Old *hæmorrhoids* of long standing which have become fibrosed may acquire a firmness suggestive of malignancy, but in this case a history of long duration should rule out the latter condition.

PATHOLOGY

Gross. The gross forms commonly assumed by epitheliomata of the lower rectum and anus have been alluded to in a previous paragraph. Regarding their location they may be divided into *internal* and *external* growths according to their origin from within or without the anal sphincters. From the point of view of morphology they may be classified as *nodular* or *ulcerating*.

Internal epitheliomata are most apt to arise and extend upward from the mucocutaneous junction, although it is apparently possible for tumors of this type to develop from a metaplasia of the cells of the mucosa. One case of this type in the sigmoid colon was observed by the author. Such a location can only be explained by a cellular metaplasia which, there is reason to believe, is brought about by irritative influences upon what would otherwise have been a columnar cell tumor. The nodular type of growth above the sphincters expands intramurally forming a flat, irregular placque or it may grow in an extraluminar fashion into the perirectal tissues without obstructing the bowel. A pedunculated intraluminar tumor may result, the pedicle of which becomes so elongated by passing fæcal contents that it is extruded with bowel movements to be manually replaced by the patient. When ulcerated the tumor grossly resembles an adenocarcinoma but does not exhibit the tendency to grow in the characteristic annular fashion of the latter. The papillomatous form is not unknown and resembles grossly a benign adenoma.

The more common *external* epitheliomata are easily divided into the two mentioned classes. The ulcerated forms first appear at the anal margin and later extend out over the peri-anal skin. They are surrounded by raised indurated edges and have dirty white or granulating bases. A cut section through such an ulcer shows that it has a hard, white, cartilaginous base which offers a definite resistance to the knife. Irregular prolongations extend downward from it into the underlying tissues. The nodular type of growth may, as has been suggested, represent an early stage of the ulcerating epithelioma but in the majority of cases it is believed, signifies a different histological tumor type. From the cutaneous surface the tumor appears as a growth which, attached to the skin, raises it in irregular nodules or retracts it in puckered ridges. The cut section shows a lobular invasion of the subcutaneous and submucous tissues arising from and thickest just beneath the epidermis. The more benign epitheliomata not uncommonly grow in a polypoid shape as illustrated in Figure 1.

The so called precancerous lesion has no characteristic gross appearance. If it be a pre-existing ulcer, fissure, fibrosed hæmorrhoid, or excrescence, there is nothing to make one suspect the presence of malignant change save perhaps an increased firmness and only by microscopical examination can the cancer be detected.

Metastases from anal epitheliomata usually appear first in the inguinal nodes, later involving the glands of the perirectal tissues and the mesorectum. Rarely are they found in distant parts of the body. This local distribution of secondary growths indicates that in all probability the deposits of cells are carried by the lymphatic channels rather than the blood stream. The distribution of metastases is explained by the course of the lymph vessels supplying the anal region. The most external portion of the anus is drained by a group of vessels which course forward in the crurascrotal region to the upper and lower tiers of inguinal nodes. Other smaller branches have been demonstrated following the gluteal fold to the same groups of nodes. The region of Hilton's white line and the lower rectum is supplied by channels following the inferior and middle hæmorrhoidal blood vessels. The former anastomose with the lymphatics supplying the rectovaginal septum and account for the occasional extension of tumors to this region. Other small branches from the lower rectum accompany the middle and superior hæmorrhoidal blood vessels. Metastases may, therefore, reach the mesorectal and sacral

glands in this manner, but since the majority of epitheliomata are situated below the latter region, these vessels are not the first to be invaded.

Microscopic. Histologically the epitheliomata of the anus are somewhat like malignant hyperplasia of the skin and mucous membranes elsewhere in the body. The tumor cells invade the basement membrane first as extensions of the malpighian pegs and later as individual ramifications, extending throughout the subcutaneous and submucous tissue. The manner of growth during this process of invasion differentiates two types of tumor. In the following discussion one type shall be referred to as the *diffuse* growth and the other as the *discrete* growth.

The cells of the diffusely growing tumor invade the tissue destroying the normal architecture and branching in every direction. They are extremely irregular in size, the nuclear diameters varying from 5 to 18 microns. The cells membranes are indistinct. The cytoplasm is faintly acidophilic and the nuclei appear as large, grayish rings rimmed with numerous chromatin particles. Mitotic figures are not especially numerous being found in from 1 to 2 per cent of the nuclei but varying in different parts of the growth. Epithelial pearls are common but vary with the age of the tumor. The keratinization is sometimes so profuse as largely to supplant the actively growing cells. The stroma is composed of loose fibrous connective and granulation tissue packed with leucocytes and small round cells. This type of cell structure is common to the ulcerating epitheliomata previously described and is illustrated in Figures 3, 4, 5, and 6.

The second type of epithelioma as depicted in Figures 7 to 10, inclusive, presents a slightly different cell morphology. The cells are attached to the malpighian pegs in the same manner but form discrete nests and strands separated by a dense connective tissue stroma. They are smaller and more regular in size, the nuclei varying from 4 to 10 microns in diameter. The cytoplasm takes a darker stain and is better differentiated. The nuclei are likewise darker and mitotic figures are found in as many as 6 per cent. Occasional giant cells are observed but no intercellular bridges or evidence of keratinization can be seen. This form resembles strikingly the basal cell carcinomata described by Krompecher and from the microscopical appearance alone the differentiation would be difficult. When correlated with the gross findings, however, it is found that the discrete type of epithelioma assumes the nodular gross form in contradistinction to the "rodent ulcer" of the face. Furthermore in the available follow-up data on this series of patients it was found that these tumors were more malignant as judged by the reappearance of the growth following excision. A resemblance may be noted between this type of epithelioma and the ramifying squamous cell carcinomata of the cervix uteri, both in the manner of growth and cellular differentiation. Furthermore, their behavior suggests a similar grade of malignancy.

Fig. 1. Case 5, Path. No. 23,880. Gross photograph of a nodular epithelioma of the anus. The growth was pedunculated but had infiltrated the surrounding skin and the presence of inguinal metastases belied the appearance of low grade malignancy.

TREATMENT

The treatment of anal epitheliomata has never been regarded as adequate. Surgeons early recognized in them a peculiarly resistant type of tumor. Accordingly, in spite of the optimism accompanying the innovation of applicable surgical procedures, palliative treatment was preferred to a mutilating operation which in the majority of cases would fail to

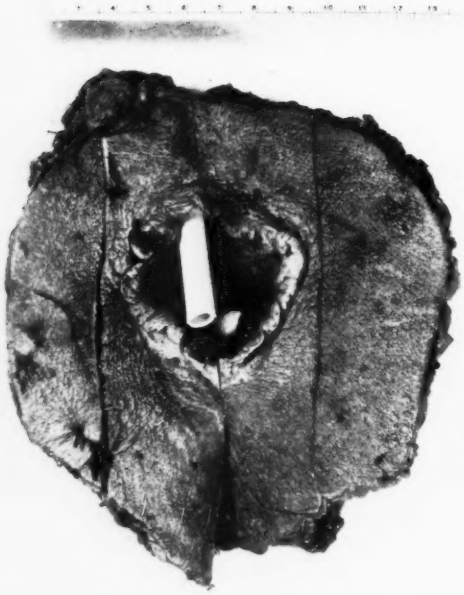


Fig. 2. Case 2, Path. No. 37,679. Photograph of specimen removed from epithelioma of the anus. This tumor was of the ulcerating type and had completely destroyed the anal aperture. The pointer is in the continuation of the anal canal. A combined abdominoperineal resection was performed, a wide margin of normal tissue being removed. The patient is well 4 years later without sign of reappearance.

effect a cure. Nevertheless, with the gradual perfection of operative technique, excision has come to be regarded less pessimistically, and although the ultimate results leave much to be desired, many now regard surgery as the only hope for permanent cure.

The early localized nodule or peri-anal ulcer is most favorable from the standpoint of curability. Even in these the mistake of conservatism is a common one. Although the growth is small and well localized the best results have been obtained by wide excision without regard for preservation of the sphincters. This may suffice for a cure but the large, ragged defect requiring months for healing and resulting in partial or total loss of sphincter control frequently causes the patient to feel that the cure is worse than the malady.

In recent years, eminent surgeons have come to favor the combined abdominoperineal operation even though the growth be small and well circumscribed. That such a radical procedure is at least partially justified is shown by the fact that the only favorable late result in this series from operation alone followed an operation of this type. This patient (Case 2) has lived 4 years after operation without signs of reappearance.

The question of routine inguinal gland dissection must necessarily be considered. This is not infrequently advocated regardless of the evident lack of metastases. The rationale of this procedure must be questioned. If the tumor cells have not begun to spread through the lymphatics, it is obvious that little will be accomplished by the dissection. If metastasis has already taken place either grossly or microscopically it is hard to conceive of the total elimination of danger since one can by no means be certain of removing all communicating lymph channels even if all affected glands are removed. To accomplish this satisfactorily the operator would be forced to remove a tremendous amount of subcutaneous tissue not only along the crurascrotal fold but from the gluteal fold as well. Furthermore extension to the inguinal glands rarely occurs until the primary growth is in a hopelessly advanced condition.

The status of irradiation in anal epitheliomata, either alone or as an adjunct to surgical extirpation, has not been sufficiently established to enable one accurately to evaluate its use. Among many other tumor groups, these neoplasms have been radiated in so few instances that it is impossible to gather enough statistics to justify conclusive deductions. Monod, of the Institut du Radium in Paris, considers them more radiosensitive than carcinomata of the rectum. Gordon-Watson of London compares the sensitivity of the tumor to that of epitheliomata of the tongue, and although he is optimistic over the results of a few personal cases, hesitates to regard any patient treated by irradiation alone as permanently cured. As is so often the case, when other methods have failed, X-ray therapy and radium have been used as a last resort.

Four of the cases in this series received some form of radiation. In Case 1, patient received heavy external radiation alone and is appar-

Fig. 3. Case 1, Path. No. 43,337. Low power photomicrograph of a diffuse epithelioma of the anus. Note the frequency of epithelial pearls and the irregularity in the growth of the cells. The stroma is scant and composed of a delicate meshwork of connective tissue fibers.

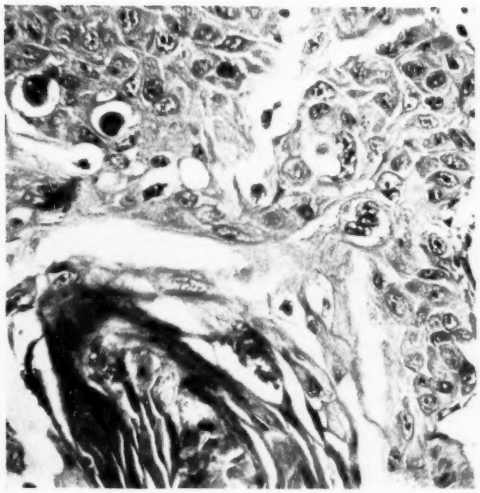


Fig. 4. Case 1, Path. No. 43,337. High power photomicrograph showing keratinization, irregularity of cells, and absence of mitotic figures. This tumor reacted well to external radiation and the patient is apparently well 2 years after treatment.

ently well today 2 years after the initial appearance of the lesion. In Case 4 patient was treated by local application of radium together with a series of 25 exposures to X-rays. The course of the growth was temporarily checked and the symptoms partially relieved, but death followed from metastases. In Case 5 patient received 35 X-ray treatments following palliative excision of the growth. She lived 3 years and was relatively symptom free until the last 6 months. The fourth patient, Case 6, was given a local application of the radium pack but became unco-operative and left the hospital. The ultimate result was not obtained.

Binkley, of the Memorial Hospital, in New York, reports 1 case in which the patient lived 7 years after irradiation alone without reappearance of the primary growth, but died from widespread metastases. Two others seen by him are apparently well at present following irradiation alone. He advocates heavy external radiation in preference to the interstitial method because of the severe reaction which not infrequently follows the latter. He feels that this followed by excision constitutes the most favorable mode of treatment.

The experience of Lenz at the Presbyterian Hospital supports Binkley's observations. He alludes to a most important factor frequently overlooked in the irradiation of tumors elsewhere in the body, namely the choice of time for the institution of X-ray therapy. Postoperative scar tissue has low resistance to X-rays and in order to prevent breaking down and radio-necrosis the dosage must be curtailed to the extent that it is frequently ineffective. To accomplish the desired result upon the tumor, massive doses are necessary. Hence Lenz advocates pre-operative irradiation in practically all instances.

To summarize we may say that anorectal epitheliomata are more radiosensitive than carcinomata of the rectum but that a permanent cure can be effected by this means is a matter of doubt. Irradiation prolongs life and ameliorates symptoms and for this reason should be emphasized in the treatment of inoperable growths. Although the primary tumor may not reappear, the growth shows a tendency to metastasize late to the inguinal nodes. It is thought that heavy external radiation followed by radical excision constitutes the best means of treatment.

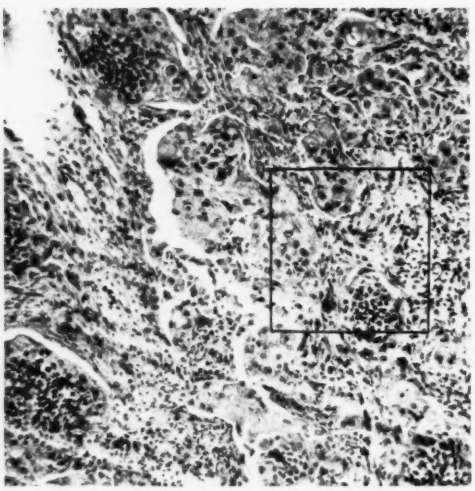


Fig. 5. Case 5, Path. No. 23,880. Low power photomicrograph of a nodular epithelioma of the anus, same case as Figure 1. The cell groups are fairly well circumscribed but the tumor possesses certain characteristics of the diffuse type of growth. Scattered throughout are peculiar groups of small, dark staining cells which are thought to represent a metaplasia of stratified squamous epithelium. This case does not conform in every respect to the typical nodular growth.

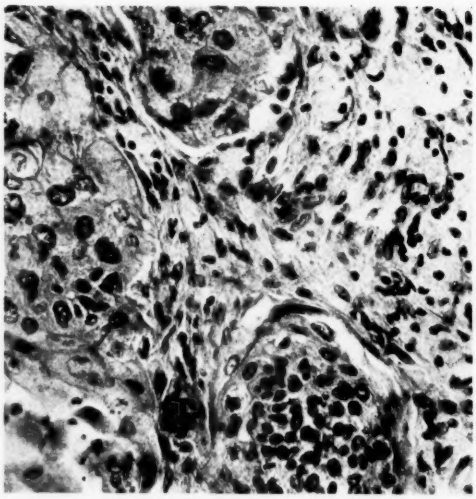


Fig. 6. Case 5, Path. No. 23,880. High power photomicrograph of a nodular epithelioma of the anus, same case as Figures 1 and 5. Note the irregularity of the size and shape of the cells and the evidence of active mitosis. There are no epithelial pearls and the stroma is quite dense. This patient had metastases in the inguinal nodes and died from metastases after palliative excision and irradiation.

SUMMARY

Ten cases of epithelioma of the lower rectum and anus have been reviewed from the standpoint of clinical features, pathology, and operative treatment.

These tumors occurred most frequently in white females in the fifth decade of life. The most common premonitory symptoms of the disease were found to be itching, pain, bleeding, and a palpable mass. Constitutional symptoms were negligible. The most frequent and constant physical findings were visible or palpable ulcers or masses and tenderness in the perineum.

The tumors commonly assumed one of two definite gross forms, either a nodular, indurating growth or a peri-anal ulcer. The first of these represented in the majority of cases a histological type characterized by cells growing throughout the subcutaneous and submucous tissues in a discrete, well circumscribed manner but showing active mitoses. The second was commonly composed of diffusely invading cells of a pure squamous type with few mitoses and many epithelial pearls. The ultimate results indicated that the former group were the more malignant.

Treatment is inadequate. Surgical extirpation, while removing the primary tumor is frequently followed by reappearance of the growth or metastases to the inguinal nodes. Irradiation frequently brings about regression of the primary growth and freedom from symptoms temporarily but patients usually die later from metastases. It is believed that external radiation followed by radical excision constitutes the optimum treatment.

In spite of the extremely poor prognosis commonly given tumors of this nature, there is no basis for assuming other than an optimistic viewpoint provided the diagnosis is made early and radical measures instituted promptly for the entire removal of diseased tissue.

CASE REPORTS

CASE 1. (Unit No. 259737.) L. M., a colored female, 48 years of age, entered the clinic complaining of pain in the rectum. This was of a sharp, scintillating character and had been present for 5 weeks. Having suffered from hæmorrhoids for a number of

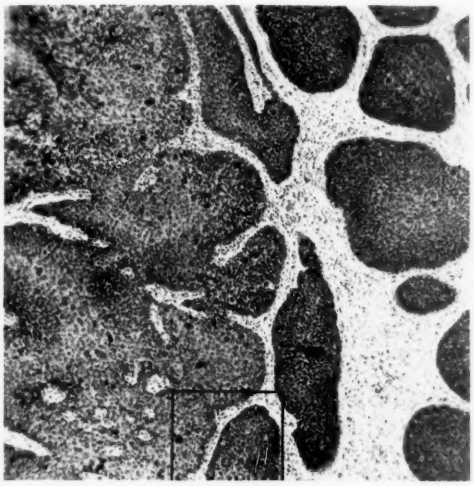


Fig. 7. Case 3, Path. No. 32,528. Low power photomicrograph of an epithelioma of the anus which was thought to have developed as a result of X-ray burns. The cells grow in a discrete manner suggesting basal cell carcinoma, forming well marked lobules separated by a dense fibrous connective tissue.

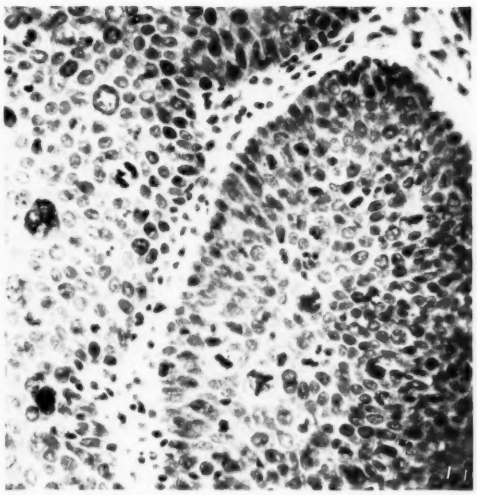


Fig. 8. Case 3, Path. No. 32,528. High power photomicrograph of tumor depicted in Figure 7. Eleven mitotic figures can be seen in this field, certainly indicating a growth of high malignancy. In spite of this the patient has remained alive for 7 years since this section was taken and shows no apparent sign of malignant growth at the present time. This was a confusing case since the only operative treatment was local excision of the skin nodules.

years she attributed the pain to that source. At the birth of her last child some months before, she had received a third degree tear into the rectum resulting in partial incontinence of fæces and urine. Examination revealed relaxation of the perineal musculature with a marked rectocele and cystocele. On the right side of the anus was found a firm ulcerated ridge with raised edges. This was 3 centimeters long and 1 centimeter wide and had infiltrated the soft tissues beneath. It bled easily to touch and superficially resembled an epithelioma. Biopsy was advised and performed.

Operation was done June 25, 1930. (Biopsy, Path. No. 43337.) The pathologist reported squamous cell carcinoma from the section.

Postoperative course. Treatment of the epithelioma was considered more urgent than repair of the perineal tear. Accordingly, since there were no available beds at the time, she was sent to another hospital. Here she received a course of X-ray therapy, but the dosage and number of treatments are not known. Two years later she again reported to this hospital for repair. On examination she was found to have no sign of the tumor. There was a small cicatrix at the former site of the lesion but no ulceration and little induration. The patient remained apparently well, 28 months.

The specimen received for examination consisted of a thin flattened piece of tissue 1 centimeter in diameter. One surface was smooth and grayish in color, the other rough and hæmorrhagic. The tissue was composed of a malignant hypertrophy of stratified squamous cells growing in irregular whorls and strands. The central portions of some of these were necrotic. The cells varied tremendously in size and mitotic figures were seen in roughly 1 per cent of the nuclei. The cytoplasm was eosinophilic, and the cell borders were not clearly marked. The stroma was composed of loose fibrous tissue heavily infiltrated with leucocytes and small round cells (see Figs. 3 and 4).

Diagnosis: squamous cell epithelioma of the diffuse type.

CASE 2. (Unit No. 71526.) G. F., a white female, aged 61 years, entered the hospital on May 15, 1928, complaining of an ulcer in the anal region. Nine months before this she had undergone an operation at another hospital for the removal of three small indurated lumps. These had been diagnosed condylomata and the condition was regarded as benign. Following the operation there appeared a residual ulcer at the site of incision, which failed to heal under conservative treatment. She had received at that time some radium but the exact dosage was not known. She had been warned against the possibility of cancer and came to this hospital for advice and treatment. Physical examination was negative except for the rectal findings. Along the posterior commissure of the anus there was a deep ulcer 5 by 8 centimeters in size. The proximal portion extended within the anus. The edges curled over a hard cartilaginous base which exuded a foul smelling, sero-

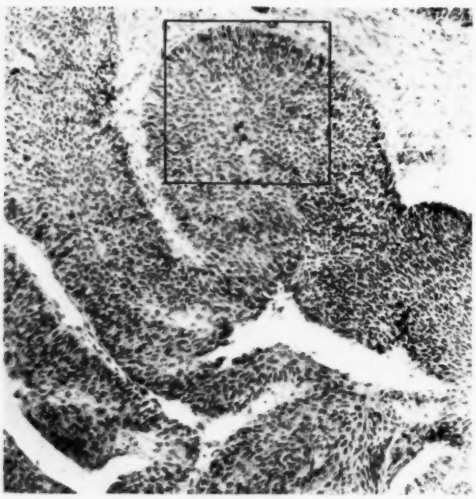


Fig. 9. Case 8, Path. No. 17,233. Low power photomicrograph of an epithelioma of the lower rectum. The cells grow in well circumscribed strands and groups separated by a fairly dense fibrous tissue. Its morphological structure is strikingly like that of basal cell carcinoma. The tumor reappeared after excision and caused the death of the patient 21 months after operation.

purulent discharge. Rectal examination was impossible on account of the pain induced.

Operation was done June 16, 1928, and consisted of a combined abdominoperineal resection. An incision was made about the anus well beyond the margin of the ulcer. The incision was carried through skin and subcutaneous tissues and the rectum was dissected free together with a large wedge shaped piece of tissue including the sphincters. The dissection was carried as high as possible and the rectum divided, the proximal stump being inverted and closed tightly. The perineal defect was then packed and the patient's position reversed on the table. Through an abdominal incision the rectal stump was drawn up and a permanent colostomy made.

The patient made an uneventful recovery. The wound healed by granulation and was almost entirely closed at the time of her discharge on July 4, 1928. She was seen at intervals of 3 to 4 months since that time and has shown no signs of recurrence. She has been well for 4 years.

The operative specimen consisted of a piece of skin 13 centimeters in diameter surrounding the anus and attached to 15 centimeters of normal rectum. On one side of the anus there was a large, deep, penetrating ulcer with a hard papilliform base. The cut sections showed extensions from this penetrating the tissues beneath. Attached to one portion of the specimen was a piece of vaginal wall which, however, did not appear to be invaded by the tumor (Figure 2).

The stained section (Path. No. 37679) showed a diffuse invasion of the tissues by irregular strands of epithelial cells. These were squamous in type, irregular in size, and showed mitotic figures in about 1 per cent of the nuclei. There was no tendency toward pearl formation. Throughout the entire section there was a profuse infiltration of small round cells and leucocytes.

Diagnosis: Squamous cell carcinoma of the anus, diffuse type.

Case 3. (Unit No. 63159.) On June 16, 1925, M.D., a white female of 39 years, first came to the clinic. The onset of her symptoms dated back to 1906 when she first noticed an intense itching in the perineal region and at the same time, a small draining sinus to one side of the anus. The discomfort persisted intermittently until 1910, when an abscess formed at the site of the fistula. This was treated by a local physician but proved to be especially resistant to healing and remained as a chronic draining sinus. During the course of the next 10 years, she consulted many private physicians and hospitals seeking relief but was not permanently helped. In 1920, she received a course of X-ray treatments lasting over a period of 7 months although the number of treatments and dosage is unknown. Following this, the itching was relieved but it was found that she had developed X-ray burns over the anus, vulva, and the backs of the hands where she had exposed them while retracting the buttocks during treatment. She first visited this hospital 5 years later. At this time the complaints were return of the itching, pain, bloody discharge, and lumps at the margin of the anus. Examination revealed a contracture of the anus with extensive scarring on either side. In the anterior right quadrant was found a tiny fistulous opening which barely admitted the tip of a probe. Bordering the anus, could be seen and felt several hard polypoid masses resembling fibrosed hæmorrhoids. They were thought to be old hæmorrhoidal tags and excision advised.

Operation was done June 16, 1925. The external hæmorrhoids were excised. The pathologist reported malignant change in the excised tissue.

After hospitalization for a few days to recover from the effects of general anæsthesia, the patient was discharged with instructions to report to the out-patient department.

The patient returned July 1, 1925 for routine follow-up. It was found that the hæmorrhoidectomy wound was healed but there was at the anal margin a small mass which had either recurred or escaped observation at the first operation. This was excised under local anæsthesia.

A fistulous tract persisted at the time of her next visit on July 15, 1925. A biopsy of this tract again showed definite malignancy. In view of this wide excision was advised but was postponed because of the presence of infection, and treatment was directed toward cleaning up local infection.

She was next seen on August 14, 1925. Her general condition was improved but the presence of en-

larged inguinal nodes was thought to indicate metastases and, therefore, inoperability. Nevertheless a gland excised for diagnosis was negative for cancer. The case by now presented a perplexing situation. If the pathological diagnosis had been correct, it was difficult to understand the prolonged life of the patient when the fistulous tract had not been completely removed. In view of this no further operative procedure was attempted at the time.

On January 8, 1926, at routine examination the anal condition was found to be entirely satisfactory but hypertrophic telangiectases had appeared over the vulva. In addition several scaly keratoses were found over the vulva and hands. These were regarded as results of the X-ray burns.

For nearly 2 years thereafter the condition changed little if at all. The itching returned and she suffered from occasional lower abdominal cramps. When seen on January 3, 1928, the lesions over the vulva had increased in size and were thought to be malignant. She was admitted to the hospital and on the following day the entire vulva was excised. The pathologist again reported malignancy on the basis of an X-ray burn. The wound healed without complications and the patient was discharged improved.

No further symptoms were produced until March 31, 1931, when the inguinal nodes again became enlarged. With the suspicion of metastases, one was excised for diagnosis but as formerly, showed nothing more than a chronic adenitis. The itching recurred a few months later and on examination a small ulcer was found in the left anterior quadrant. She was admitted for a third time and the ulcer excised. It was again reported "transitional epithelioma." The wound failed to heal entirely and she was admitted a fourth time for wide excision. This time a biopsy showed nothing but inflammatory tissue. The wound healed nicely with proper care and the patient, still in good general health was discharged.

During the past year she has been seen on several occasions but there has been no recurrence of symptoms nor has the growth reappeared. On August 16, 1931, a complete examination of the large bowel was made including a barium enema and sigmoidoscopic examination, but no abnormality was found. At present her general health is good. The Wassermann reaction was negative on several occasions.

Result: She has been well 7 years.

There was nothing characteristic in the many small bits of tissue removed for diagnosis (Path. Nos. 46255, 37164, 32528, and 32597). Most of them were small pieces removed at biopsy. The specimen removed on January 5, 1928, consisted of the entire vulva including the labiæ minora and the clitoris. These were hyperæmic and ædematous and near the posterior end of the right labia was seen a definite ulceration 1 centimeter in diameter with rolled edges and an indurated base. Several bluish areas of telangiectasis were scattered over the entire surface of both labiæ.

In general all of the specimens removed from the ulcerated areas showed the same type of epithelial proliferation. There was a thickening of the epidermis with hyperplasia of the malpighian pegs which in some places had broken through the basement membrane and infiltrated the underlying tissues. It is possible that this might have occurred in a benign overgrowth of epithelium but in the presence of abundant mitotic figures (from 4 to 6 per cent of the nuclei) its malignancy could hardly be doubted. The cells grew in discrete groups and resembled in some ways a basal cell epithelioma. No pearls were found. Sections taken through the telangiectatic areas showed dilated and thrombosed vessels. It was thought that the growth on the vulva was a new lesion developing after an X-ray burn and not an extension of the primary growth at the anus (see Figs. 7 and 8).

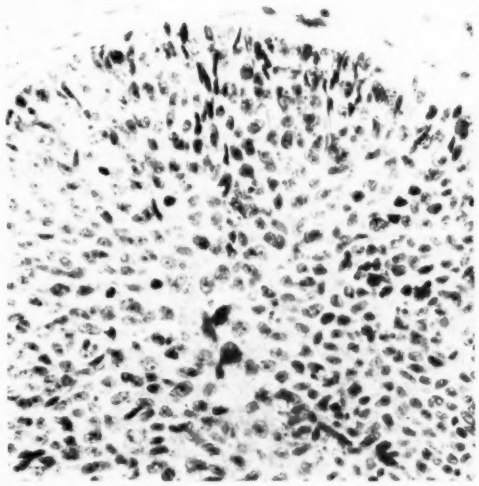


Fig. 10. Case 8. Path. No. 17,233. High power photomicrograph of the tumor shown in Figure 9. This shows a fair uniformity of the size and shape of the cells and the presence of a few mitotic figures. Although this does not impress one as a tumor of high grade malignancy, the patient died from reappearance of the growth after excision.

Diagnosis: Squamous cell epithelioma of the anus of the discrete type following X-ray burns.[1]

CASE 4. (Unit No. 61010.) W. O., a colored male, aged 76 years, was admitted to the hospital on September 29, 1924, complaining of rectal bleeding for 2 months. Coincident with the onset of the bleeding he had noticed a small mass in the lower rectum which was sometimes palpable after a bowel movement. This was slightly tender and caused him moderate discomfort by obstruction to passing fæces. On physical examination nothing could be seen externally. Examination of the rectum revealed

[1] It is questionable if this tumor arose from the true anal epithelium or the skin of the perineum. In spite of its atypical behavior the gross and microscopic characteristics were those of anal epitheliomata and the consensus of opinion favored the former origin.

a hard mass on the anterior wall extending from the anal margin to the prostate. Over the center of this was a furrow into which could be laid the palpating finger. Induration at the lower end of the growth extended out under the skin for a distance of 2 or 3 centimeters, and could best be appreciated with one finger in the rectum and another exerting pressure on the perineum. Examination of the stools on one occasion showed the fæces normal in consistency and color and negative for occult blood. The Wassermann reaction was negative.

Operation consisted in curettage of the sinus. In curetting the growth the mass was found to be firmly fixed and attached to the prostate. Considerable resistance was met with by the instrument, giving the operator the impression of an extremely hard growth.

Following the operation 100 milligrams of radium in a rubber tube was inserted in the sinus, being held in place by a gauze pack. This was removed after 3 hours. The patient was discharged unimproved but returned to the out-patient department for a series of X-ray treatments. During the following 7 months, he received 25 treatments from a 200 kilovolt machine. The anode skin distance was 50 centimeters and the rays filtered through 0.5 millimeter copper and 2 millimeters of aluminum, the dosage consisting of 90 to 180 milliampere minutes. The general condition of the patient improved as a result of this treatment, but he did not become entirely symptom free. He continued to have pain and a persistent bloody, mucous discharge. He was readmitted on June 3, 1925, for these symptoms. A small sinus at the anterior margin of the anus discharged a foul smelling seropurulent fluid. A palliative colostomy was considered but thought inadvisable. Accordingly the patient was discharged unimproved after 1 week of observation.

He was not followed.

The tissue received consisted of a few shreds removed at biopsy and were not characteristic in appearance (Path. No. 31198).

The tumor was composed of pavement epithelial cells growing in a circumscribed manner, forming nests and strands well delineated from one another. The cells were relatively small but varied a great deal in size and shape. Mitotic figures occurred in about 2 per cent of the nuclei. The stroma was scanty and most of the section was taken up by the actively growing cells. There was very little secondary infiltration.

Diagnosis: Squamous cell epithelioma of the discrete type.

Case 5. (Unit No. 45128.) L. H., a colored female, 59 years of age, was admitted to the hospital on January 5, 1920, complaining of a growth in the rectum and vagina. Her attention had been first called to it 1 year before, and it had since then grown progressively larger. The mass caused a dull dragging pain in the lower pelvis which was somewhat relieved by hot applications and baths. Rectal hæmorrhages had occurred every few weeks since the onset of symptoms and during the last of these about a week before admission approximately a pint of blood had been lost. She felt that on occasions the pressure of the mass caused a moderate dysuria. Some weight had been lost during the latter 9 months of her illness but the exact amount was not known. Physical examination revealed a hard irregular mass extending from the anus to the posterior portion of the vulva, which had begun to infiltrate the surrounding perineum. The left labia was moderately hypertrophied and œdematous. The tumor mass had not extended into either the rectum or vagina. The Wassermann reaction was negative. The condition was diagnosed epithelioma of the anus and, although no metastases were evident, the size of the growth was regarded as indicative of inoperability. Nevertheless it was felt that a palliative excision would partly relieve her symptoms.

Operation was done March 1, 1920, and consisted in a palliative excision of an epithelioma of the anus. The excision was carried wide of the mass and included a part of the anal margin and sphincter. A rectal tube was inserted and the wound closed without drainage.

The wound broke down on the eighth day after operation but thereafter healed by granulation. The patient was discharged on March 24, 1920, improved, but with partial loss of sphincter control. X-ray treatment was instituted and over a period of 2 years a total of 35 treatments were given with a voltage of 80 kilovolts, at an anode skin distance of 25 centimeters, in doses varying from 5 to 60 milliampere minutes with 4 millimeters aluminum, 1 centimeter wood and 2 millimeters bakelite filters. This was efficient in relieving the patient of all pain and bleeding but the subsequent appearance of nodules in the vulva precluded a hopeful prognosis. About 2½ years after the operation, the patient again began to suffer from pain and dysuria. Thereafter her course was steadily downhill and she died on March 20, 1923, almost 3 years after her first admission to the hospital.

The specimen (Path. Nos. 23880 and 24072) consisted of a wedge shaped piece of tissue 10 by 5 by 2 centimeters, the outer surface of which was covered by skin. From this projected two nodular elevations, one of which seemed to be undergoing degeneration. These masses offered resistance to the knife when cut and exposed a grayish white tissue studded with yellow spots. The consistency was of cartilaginous density (see Fig. 1).

The tissue was composed of a malignant hypertrophy of squamous cells growing in discrete sheets and groups with a minimal stroma. These were large and irregular both in size and shape. Necrosis was marked in the centers of some of the cell groups, but there was no tendency toward pearl formation. Mitotic figures were found in less than 1 per cent of the nuclei (see Figs. 5 and 6).

Diagnosis: Squamous cell epithelioma of the discrete type.

CASE 6. (Unit No. 38830.) I. M., a white female of 41 years, entered the hospital on August 1, 1918, complaining of pain in the rectum. Ten weeks before a swelling had appeared on the right side of the anus which was thought by her local physician to be an abscess, and opened. This healed but the swelling returned and with it pain appeared. She could not sit without a great deal of discomfort and defæcation caused her extreme pain. She had attributed occasional dysuria to the presence of the mass. Physical examination showed a mass on the right side of the anus dissecting into the perineum and out beneath the skin of the buttocks, making rectal examination extremely painful. The mass was red and tender and extended from the rectum to the vagina. It appeared grossly to be an abscess and at one point there was a small fistula from which pus was escaping. A cursory rectal examination revealed some swelling and induration inside the rectum. Malignancy was suspected and biopsy advised. In view of the pain on defæcation it was thought advisable to perform a palliative colostomy.

Operation was done August 3, 1918, and consisted in colostomy and excision of perineal sinus with division of the sphincter. The pathological report showed malignancy in the section and the case was regarded as inoperable.

Postoperative treatment consisted in the application of 100 milligrams of radium in a rubber tube inserted in the operative wound, but this fell out after 3 hours and was not replaced. She was discharged 3 weeks after the operation somewhat improved. The colostomy was working well and the symptoms were relieved. The patient was seen once 2 months later by a visiting nurse who reported progress of the malignant condition. Due to lack of co-operation by the family subsequent visits were unfruitful and the case was dropped.

The specimen (Path. No. 21641) received in the laboratory consisted of two small pieces of tissue, each about a centimeter in diameter, evidently comprising a portion of the sinus tract.

The section was composed largely of fibrous tissue bordered by epithelium on one side. Throughout the abundant stroma could be seen a diffuse proliferation of epithelial cells varying tremendously in size and shape. These grew in an irregular manner and preserved no distinct line of demarcation from the surrounding tissue. A few pearls were seen and other evidence of early keratinization. Mitotic figures were present in less than 1 per cent of the nuclei.

Diagnosis: Squamous cell epithelioma of the diffuse type.

CASE 7. (Unit No. 20962.) J. M., a white male aged 45 years, was admitted to the hospital on July 6, 1915, complaining of pain in the perineum. The onset of symptoms 8 weeks before was marked by the appearance of a small abscess just outside the anal margin which ruptured spontaneously and healed in about a week's time. Following this the patient began to suffer from a dull dragging pain in the lower pelvis which change of posture would not relieve. This became severe enough to keep him awake at night. Frequency of defæcation and tenesmus were associated with the pain. Physical examination showed an elderly white man who was made irritable by the constant presence of pain. Nothing could be seen or felt on external examination of the anus but on digital examination of the rectum a firm hard ridge could be felt beginning just within the anus on the anterior wall and extending upward to the prostate and the retrovesical pouch. The Wassermann reaction was negative. The condition was thought to be malignant and resection was advised.

Operation was done July 10, 1915. Through a preliminary colostomy, a brief exploratory examination revealed no metastases.

On July 20, 1915, a partial resection of rectum was done. The coccyx was removed through a sacral incision and the rectum was dissected free for a distance of 3 inches above the sphincters. At this point the condition of the patient became so bad that the tumor was separated from the prostate rapidly, leaving the operator uncertain as to whether he had removed the growth *in toto*. The wound was closed and the patient left the table in poor condition.

The patient was in a severe state of shock following the operation from which he did not recover and succumbed 2 days later to myocardial failure.

The tissue (Path. No. 17319) removed at operation consisted of a portion of the rectum with the anus. When this was opened there was seen on the anterior surface an elongated tumor mass which had indurated but had apparently not extended beyond the wall of the bowel. This was firm and, when cut, exhibited a dense fibrous consistency. The upper end of the tumor had been cut across during its removal so that it was evidently only partly removed.

The tumor was made up of groups of cells growing in a circumscribed manner in a scant but dense stroma. They were relatively small but variable in size. No pearls were seen and mitotic figures occurred in less than 1 per cent of the nuclei. The cells were apparently of epidermal origin and grew in a manner suggesting basal cell carcinoma.

Diagnosis: Squamous cell epithelioma of the anus, discrete type.

CASE 8. (Unit No. 23195.) E. M., a white female aged 43 years, was admitted to the hospital on March 22, 1915, complaining of hæmorrhoids and occasional bleeding from the rectum, over a period of 5 weeks. Pain was a prominent factor and was accentuated by bowel movement or by sitting down. It was increased by constipation and relieved by diarrhœa. Her appetite was poor and she had lost a moderate amount of weight. Physical examination showed a well nourished woman without appreciable signs of malaise. The abdominal findings were negative except for a moderate amount of right lower quadrant tenderness. Rectal examination revealed an obstruction in the form of an annular stricture just above the sphincter above which could be felt

several small polypoid growths. The condition suggested malignancy and a biopsy was performed.

Operation was done March 24, 1915, and consisted in dilation of stricture and biopsy of growth. The pathologist reported a malignant tumor of the squamous cell type.

A radical operation was advised but was refused by the patient. Accordingly she was discharged and referred to a convalescent home. She returned to the hospital 2 months later with symptoms practically unchanged, having decided to submit to the operation. The symptoms and signs had changed very little in the interval.

A preliminary colostomy was done June 2, 1915.

On June 23, 1915, perineal proctectomy was performed. After making a linear sacral incision the operator first removed the coccyx then dissected the rectum free 6 inches above the tumor where it was divided. The anus was then divided with a narrow margin of skin and the tumor was removed intact. The wound was packed and allowed to heal by granulation.

The perineal wound closed slowly and the patient was discharged on September 13, 1915, with the colostomy working satisfactorily. For over a year the patient lived and was symptom free. About 14 months after the operation, however, symptoms recurred and from then on the course of the disease was steadily downward. She died 21 months after the operation from a reappearance of the tumor.

The specimen (Path. Nos. 17233 and 16877) removed at operation consisted of the rectum and the anus. At the anal margin were several hæmorrhoids. On the posterior wall of the lower rectum about 2 centimeters above the sphincters was seen a hard indurated projection into the lumen of the bowel. This extended about half way around the gut but did not entirely obstruct it. Ulceration was starting in one place. Several enlarged glands were found in the perirectal tissues posterior to the tumor. On cutting through the mass it was found to be hard and glistening. White strands extended through all coats of the rectal wall. The lymph glands were yellowish white in color and contained minute white cystic spaces.

The tumor was composed of malignant squamous cells densely packed together in a cellular fibrous stroma. They formed discrete groups which were well circumscribed. The cells were large and the nuclei varied in size from 6 to 12 microns in diameter. Mitotic figures were found in less than 1 per cent of the nuclei, and although no pearls were seen, the cells were relatively well differentiated. Occasional giant cells were found, some of which contained two or more nuclei. The sections taken from the lymph glands showed the normal structure almost entirely replaced by cells of the same type as found in the original tumor (see Figs. 9 and 10).

Diagnosis: Squamous cell epithelioma of the lower rectum, discrete type.

CASE 9. (Unit No. 20584.) L. M., a white female, 42 years of age, entered the hospital on January 25, 1915, complaining of rectal bleeding for 2 months. This was preceded several months by weakness, dyspnœa, and headaches which she felt were not related to the melena. The bleeding was intermittent at intervals of from one to several days and on a few occasions was copious. Weakness had increased during the month previous to admission. Examination showed the abdomen slightly distended and tender to palpation throughout. At the anal margin were seen several hæmorrhoids and 2 centimeters above the sphincter was felt a narrowing of the lumen similar to a muscular contraction. The hæmoglobin was 40 per cent. Proctoscopic and sigmoidoscopic examinations were negative. The case was diagnosed hæmorrhoids and excision advised.

On January 27, 1915, the external hæmorrhoids were excised. Two large polypoid masses were clamped and excised with a cautery. During this process a depression was seen just within the sphincter which was covered by dark tissue and contained a small ulceration at the base. A piece of this was excised for diagnosis.

The patient was discharged 2 days later. The pathological report which was received after discharge was carcinoma. It was impossible to get in touch with the patient and the case was dropped. She returned 3 months later with an exacerbation of symptoms. In addition she was suffering from lower abdominal pain. There was no evidence of any extension of the ulcer noted on previous examination. Exploratory laparotomy was thought feasible.

Operation was done March 1, 1915, an exploratory laparotomy. The findings were entirely negative and nothing was found to account for the symptoms. The bleeding was attributed to internal hæmorrhoids.

The patient recovered without complications and was discharged improved symptomatically. Blood was seen in the stools only twice during convalescence. Following discharge the patient failed to report for follow-up and the ultimate result is not known.

The material (Path. No. 16654) received from the biopsy consisted of a few small shreds of tissues. There was nothing characteristic in the gross appearance.

The tissue was made up of homogeneous groups of squamous epithelial cells grouped about central degenerating areas. The cells were small, varying from 4 to 9 microns in diameter. Mitoses occurred in less than 1 per cent of the nuclei but the cells appeared to be definitely malignant. The stroma was scanty but infiltrated by many leucocytes.

Diagnosis: Squamous cell epithelioma of the anus, diffuse type.

CASE 10. (Unit No. 5893.) A. P., a white female aged 48 years, was admitted to the hospital complaining of rectal bleeding. She had noticed blood in the stools on one occasion 15 years before but it did not recur until 1 year before admission. At that time she had a moderately severe hæmorrhage accompanied by a sensation of something giving way. At first the bleeding was intermittent every few

TABLE I.—SUMMARY OF DATA ON TEN EPITHELIOMATA OF THE LOWER RECTUM AND ANUS

Case	Location	Gross type	Microscopic type	Treatment	Result
1	Anus	Ulcerative	Diffuse	X-Ray	Living, 2 yrs.
2	Anus	Ulcerative	Diffuse	Abdominoperineal resection	Living, 4 yrs.
3	Anus	Nodular	Discrete	Local excision	Living, 7 yrs.
4	Lower rectum	Nodular	Discrete	X-ray and radium	Not followed
5	Anus	Nodular	Diffuse	Palliative excision and X-ray	Dead, 36 months from reappearance of tumor
6	Anus	Ulcerative	Diffuse	Palliative colostomy, radium	Not followed
7	Lower rectum	Nodular	Discrete	Perineal excision	Dead from postoperative shock
8	Lower rectum	Nodular (with secondary ulceration)	Discrete	Perineal excision	Dead, 21 months from reappearance of tumor
9	Anus	Ulcerative	Diffuse	None	Not followed
10	Lower rectum	Ulcerative	Diffuse	Perineal excision	Dead from postoperative shock

weeks but during the last 5 months of her illness some blood appeared with almost every stool. For 4 months she had suffered from a constant dull pain in the rectum which was worse when she sat or lay down and was relieved by walking or moving about. Weakness and fatigability contributed to the condition and she had lost a moderate amount of weight. On examination a small protrusion was seen at the anal margin which resembled a hæmorrhoidal tag. Digital examination of the rectum showed a collar shaped growth beginning at the mucocutaneous border and extending upward about 4 centimeters. The surface was rough, and bled easily to touch. It was freely movable, and there was no evidence of extension. The condition was diagnosed carcinoma of the rectum and radical extirpation was advised.

On April 29, 1908, perineal resection of the rectum was done. Through a linear incision from the anus to the sacrum the coccyx was removed and the rectum dissected free. A circular incision was then made about the anus and the bowel freed to a point 1 inch above the tumor. The bowel was divided at this point and the lower end brought down and sutured to the skin edge.

The patient was in poor condition when she left the operating room. She went into shock from which she never recovered and died on the following day.

The specimen (Path. No. 8252) removed at operation consisted of the lower rectum and anus. Just inside the anal orifice was found an annular tumor 5 centimeters in length. The surface was ulcerated and the consistency was hard and fibrous.

The section showed large masses of epithelial cells infiltrating the entire rectal wall in poorly defined groups. In some places the cells were stratified, in others cuboidal, but throughout there was marked irregularity in both size and shape. Mitotic figures were found in about 2 per cent of the nuclei. The stroma was scanty and loaded with leucocytes. The tumor cells were poorly differentiated and indicated a tumor of relatively high grade malignancy.

Diagnosis: Squamous cell epithelioma of the lower rectum, diffuse type.

BIBLIOGRAPHY

1. Allingham, W. Diseases of the Rectum. London: Churchill, 1879.
2. Binkley, G. E. Personal communication.
3. Bushe, G. A Treatise on the Malformations, Injuries and Diseases of the Rectum and Anus. New York: French & Adlard, 1837.
4. Cutting, R. A. Carcinoma of the anus and rectum. Am. J. Surg., 1930, x, 547.
5. Desault. Clinique Medicale, suivie, d'un Traite des Maladies Cancereuse, p. 148, Paris, 1833.
6. Drueck, C. J. Types of anal and rectal cancer. Internat. Clin., 1927, i, 196.
7. Gant, S. G. Diseases of the Rectum, Anus and Colon. Philadelphia and New York: W. B. Saunders Co., 1923.
8. Goodsall, D. H., and Miles, W. E. Diseases of the Rectum and Anus. New York: Longmans, Green and Co., 1875.
9. Gordon-Watson, Charles. Personal communication.
10. Lynch, J. M. Epitheliomata of the rectum and anus. J. Am. M. Ass., 1917, Nov. 24.
11. Makins, G. H. A case of mixed carcinoma and epithelioma of the anus. Brit. J. Surg., 1913, i, 332.
12. McCray, P. M. Epithelioma of the anus. Surg. Clin. North America, 1926, vi, 1623.
13. Monod, O. Personal communication.
14. Pack, G. T. The pathological aspects of anal and rectal neoplasms. Internat. Clin., 1927, ii, 77.
15. Plisson, L. Ano-rectal epitheliomata. Progress Med., 1927, xlii, 1408.
16. Van Buren, W. H. Diseases of the Rectum. New York: D. Appleton & Co., 1875.
17. Yeomans, F. C. Proctology. New York: D. Appleton & Co., 1929.
18. Lenz, Maurice. Personal communication.

DETAILED STUDIES OF A SERIES OF GALL-BLADDER CASES[1]

EDMUND ANDREWS, M.D., F.A.C.S., CHICAGO
From the Department of Surgery of The University of Chicago

IN a series of previous communications the results of experimental studies on the gall bladder were reported which may be summarized somewhat as follows: (a) Infection may easily reach the gall bladder from the rich flora of the adjacent liver (4), which acts as a filter for the many bacteria entering the body through the gastro-intestinal tract (10). (b) Cholesterol precipitation is brought about by the absorption of its solvent, the bile acids, by the diseased gall bladder (1, 9). In our use of the term "diseased gall bladder," the vagueness was intentional and it was emphasized that thus far the various factors of disease, i.e., infection, œdema, stasis, irritation from extraneous material, etc., could not be separated. (c) The normal gall bladder, in its process of concentrating the bile, does not absorb bile acids any faster than cholesterol, if at all, and hence causes no tendency to stone formation. (d) Cholesterol is not excreted by the gall-bladder mucosa in sufficient quantities to be a factor in stone formation (2). (e) Calcium is rapidly absorbed from the acutely infected gall bladder (5). (f) In spite of large numbers of experiments it could not be shown that the character of the bile secreted by the liver was of importance in the problem and the blame seemed to attach to the gall bladder (7, 13).

In the meantime the importance of cystic duct obstruction in the deposition of calcium in the bile or on stones was noted by Phemister (24), and has since been produced experimentally both by him (25) and by ourselves (2).

With these points in view pathological and bacteriological chemical studies were made of a series of 61 operative gall-bladder cases. Although in many cases the studies were for obvious reasons incomplete as can be seen from the table, the goal aimed at was to do in each case all the analyses which might throw light on the subject, and enough data have been gathered in most cases to be of value. In many of the multitudinous studies previously reported only one or two of the single factors have been investigated, the accumulation of much data on even this short series, therefore, throws new light on the subject.

PROTOCOLS

A definite technique was aimed at in acquiring the specimens. Where possible, liver bile was secured from the common duct for study. It was attempted to clamp the cystic duct as soon as possible in the course of the operation so as to prevent escape of bile from the gall bladder, and thus to get figures on the total gall-bladder contents. Another clamp was placed across the tip of the fundus to serve as a handle and the specimen was immediately delivered to the laboratory without the clamps being removed. A special attempt was made to avoid handling the gall bladder during the operation so as to avoid bleeding into it and also breaking off of the delicate villi.

The closed gall bladder was then aspirated with a fine needle to get sufficient material for culture and for hydrogen-ion determination. It was then X-rayed, aseptic precautions still being used in handling the specimen. The tip with the clamp was then cut off and divided into two portions, one for culture and the other for chemical analysis. The bladder with the clamp on the cystic duct was then placed in a bottle and filled with formalin through the hole in the fundus and after being distended thus for a few minutes, was immersed in the fixative. After hardening it was cut into rings 1 centimeter thick, and each ring was embedded in paraffin and cut. The larger ones were embedded in celloidin. It was in this manner possible to get serial sections about 1 centimeter apart from the duct to the fundus.

The bile was then centrifuged and the sediment, if any, analyzed separately. In some cases there was not sufficient bile to permit this. The analyses were made as follows: The white blood count was done by the usual method except that 1 per cent acetic acid was neces-

[1]Read before the Western Surgical Association, December 10, 1932.

sary to neutralize the alkaline bile. The bile acids were estimated according to the method of Schmidt and Dart, Koch's modification of the amino nitrogen apparatus of Van Slyke being used. Cholesterol was estimated by the method known as Bloor (11). The extraction and separation of these substances from the bile was done with petrol ether as described by us (6). It permits both analyses on 1 cubic centimeter of bile, a valuable point as many diseased gall bladders have a small bile content. Calcium estimations by the usual blood technique are not interfered with by the bile pigment which is all removed by the strong acid. The Clark-Collip modification of the Kramer and Tisdall method was used. Hydrogen-ion estimations were done by the Hastings method and the carbon dioxide by that of Van Slyke.

In the tissue analyses the bit was weighed wet and then dried and weighed again, *in vacuo* at room temperature over calcium chloride. The tissue was then ground and extracted with alcohol and ether and the cholesterol estimation made as above. For calcium, after the wet and dry weights were obtained, the tissue was oxidized and run as above. In both cases the analyses are expressed in terms of dried tissue, as this tends to rule out the factor of œdema. In a few cases the cholesterol content was estimated on preserved specimens and the results seemed to be within the same range as did the fresh specimens. Cholesterol is of course absolutely insoluble in water or formalin. On the other hand, calcium is rather soluble in acid media, so fresh specimens cannot be used.

In many cases duplicate or even triplicate estimations were done to insure the accuracy of the work. This was especially true in the difficult gas analyses where frequent checking was necessary. We are thus able to give the following estimate of the accuracy of our work which may prove of value in evaluating it: Bile acids, expressed in terms of glycocholic, exceedingly delicate, error less than 2 per cent. Bile cholesterol, very crude, margin of error about 20 per cent; tissue cholesterol, the same, with a tendency for the figures to run too low on account of incomplete extraction. In the case of the tissue calcium as well as blood calcium, variations of 0.2 milligrams per 100 cubic centimeters can be demonstrated.

The bacteriological examinations were planned to give a quantitative as well as qualitative result. The gall-bladder wall was implanted into Rosenow's brain broth, the lower portions of which acted as anaerobic media. The bile was planted into the same media and as well various dilutions of 0.1 cubic centimeter were inoculated into poured plates in order to make bacterial counts. If more than one organism was encountered in the smears, plates were poured and pure cultures secured and identified by suitable means.

ANALYSIS OF RESULTS

Grouping cases into definite types has been a matter of great difficulty on account of the lack of correlation between the criteria usually used. The total lack of any apparent relation between the cultures, the pathological findings, and the clinical histories, has in many cases been very striking. Especially confusing is the fact that the gross findings at operation so frequently fail to fit in with the microscopic picture. In addition the finding of sterile bile and gall-bladder wall in many clinically acute cases gives food for thought. Only the most elementary classification into types has therefore been possible, and even this requires explanation.

1. *The normal gall bladder* (Table I). This group includes cases with normal or nearly normal gross and histological findings with no stones, 6 cases. Three patients had had typical afebrile colics, one with jaundice. All were operated upon during intervals. The absence of findings together with the fact that all 3 were relieved of their colics makes it probable that all had passed their stones. One patient was a diabetic with beginning cirrhosis of the liver and a few mild attacks. At the request of Dr. Russel Wilder a cholecystectomy and drainage of bile was done. Another was operated upon with a history of mild afebrile colics, which, though hardly sufficient to warrant operation *per se*, corresponded with a severe flare-up of arthritis deformans. The sixth had had quite severe acute attacks with fever. Non-visualization with intravenous dye had previously been noted. She was operated

TABLE I

	Case No.	Type	Last colic	Last fever	Last jaundice	X-ray	Operation	Gross pathology			Sections	Calculi
								Cystic	Common	Gall bladder		
		1	2	3	4	5	6	7	8	9	10	11
Normal	42551	Severe colic 1 mo. ago, fever	3 days	1 month	1 month	—	E	P	P	Œdema?	N-1	0
	54970	Many afebrile colics	Weeks	0	0	—	E	P	P	Normal. Healed gastric ulcer	N	0
	34963	Diabetes, cirrhosis, mild colics	Weeks	0	0	NV	E with drainage of common	P	P	Thick, adherent	1	0
	38510	Many mild afebrile colics	3 days	0	0	NV	E	P	P	Thin	N	0
	67709	Old history repeated colics	Old	0	?	NV	E	P	P	Slightly thick glands	N	0
	68098	Very mild colics, removal arthritic focus	Slight	0	0	NV	E	P	P	Normal	N	0
Normal with stones	53692	Previous G.B. drainage, recurrent pain	0	0	0	NV 2 large Ca	E	P	P	Normal except adhesions	N	3 chol. Ca in cracks
	32259	Many severe colics. Pancreatitis?	2 weeks	0	0	—	E	P	P	Normal	N	Hundreds of small chol. stones
	26691	Duodenal ulcer and few colics	Old	0	0	Faint vis.	E	P	P	Normal	N	20
	65860	Catarrhal jaundice. Repeated atypical colics	Recent	0	0	Faint vis.	E	P	P	Normal	N	41 chol. few traces Ca
	62613	Numerous typical colics	Old	0	0	Flat plate large Ca stone	E	P	P	—	N	4
Jaundice	55249	20 years colics now jaundiced	Few days	?	+	—	E	P	P	Adhesions distended	N	0
	44942	Silent jaundice	0	0	++++	—	Cholecystgastrostomy	P	C	Thin distended ca, pancreas	0	0
	44040	Silent jaundice	0	0	+	Neg. G.I.	Cholecyst enterostomy	P	C	Thin distended ca, pancreas	0	0
	55801	Pancreatitis? PM suppurative portal-phlebitis	Active	+	+	Flat plate neg.	Cholecystostomy	P	?	—	0	1 homogenous chol.
	36958	Charcot intermittent fever	Active	+	+	Flat plate neg.	E with stone in common and hepatic	C	C	Thick adhesions	2	50 chol.

Column 5. NV, normal visualization.
Columns 7, 8. P, patent; C, closed.

upon in an interval, and the absence of any pathological findings was a surprise. Unfortunately no follow-up report is available on this patient. While it cannot be said that these patients were normal as the five followed were cured, the total absence of operative findings justifies the statement that they were at least quiescent at the time of operation.

2. *Normal gall bladder with stones* (Table I). This group is self-explanatory. It includes 5 cases. Two were in all likelihood silent stones as the symptoms could easily be explained by other causes, one duodenal ulcer and one colitis. The 3 others were quiescent at the time operation was done as they had had typical biliary colics. In all 5 the gall bladder was thin walled, the cystic duct patent, and the stones of the multiple facetted cholesterol type, 2 having slight calcium rings about them.

3. *Jaundice* (Table I). In this group are placed 5 cases with common duct obstruction but with the cystic duct patent. In those jaundiced patients with the cystic duct closed, it was obvious that the jaundice was not an

TABLE I

Bile								Sediment		Total in G.B.		G.B. Wall		Cultures		P.O. Reaction	
c.cm.	W.B.C.	B.S.	Chol.	BS/Chol.	Ca	CO_2	pH	Chol.	Ca	Chol.	Ca	Chol.	Ca	Wall	Bile		
12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
15		2275	33	69						4.95				S	S		
11	1892	2390	236	10	46.3	20	6.84	0		25.96	5.09			S	S	0	
		1130	69	16	21			0		2.76	.84			Staph. albus	S	0	Normal
14	3000	5459	143	38	30.2	26.3	7.1	.095		20	4	1080	380	B. welchi	B. welchi 1–5 per c.cm.	0	
10	2000	3473	167	21		26	6.9			16		960	570	S	S	±	
18		5373	300	18	35	40.5				54	6.3	200	140	B. welchi	S	±	
1		2694	220	12										B. welchi	S	±	
		175	78	2	25.7											±	Normal with stones
2.5	1225	870	89	10						2.2		330	56	B. coli staph.	B. coli, staph. 350	±	
7	2346	2695	95	28	20.2			1.46		8	.14	850	840	Gram and diphtheroids	Gram and diphtheroids 2010	±	
40	4000	1828	183	10	17	26	7.07	.63		74	6.8	138	30	S	S	0	
18	2132	2560	288	9	29	30	6.82	.006		51.8	3.9			Few staph.	S	±	
		1994	200	10												0	
15		2949	65	45												Died	Jaundice
17	1936	835	75	11	23.9			.00026							B coli	Died	
														B. coli B. welchi	B. coli B. welchi	Died sepsis	

Column 12. c.cm. of bile. Exact in closed ducts. If duct open, some often escaped during operation.
Column 13. Figures show number per c.cm. of uncentrifuged bile.
Columns 14, 15. Figures in mg. per 100 c.cm.
Column 18. Vol. per cent.
Columns 20, 21. Total content in mg.
Columns 22, 23. Total in mg. exclusive of stones.
Columns 24, 25. Mg. per 100 gm. dry wt.
Columns 26, 27. S, sterile.

appreciable factor in determining the gall-bladder contents and therefore they are placed in the acute group. These 5 included 2 carcinomata of the pancreas in which the gall bladder was anastomosed to the stomach or bowel, 1 case of suppurative portal thrombophlebitis, 1 of common duct stones, and 1 in which the cause of the obstruction could not be ascertained, but was probably a stone passed just prior to the operation as the patient was cured after cholecystectomy.

4. *Acute cases* (Table II). This group includes all those showing signs of activity at or immediately before the operation. This activity was evidenced by pain, with or without jaundice, fever, or leucocytosis, or the finding of fresh fibrinous exudate or typical pathological pictures of acute inflammatory process.

TABLE II.—ACUTE

Case No.	Type	Last colic	Last fever	Last jaundice	X-ray	Operation	Gross pathology			Sections	Calculi
							Cystic	Common	Gall bladder		
	1	2	3	4	5	6	7	8	9	10	11
50635	Ca. pancreas	o	?	++++	Flat plate neg.	Cholecyst-gastrostomy	C partly	C	G.B. distended	o	o
57846	Active acute colic	3 days	4 days	Old	Flat plate neg.	E	C	P	Thick, tense hepatitis	2	10 chol.
23335	Repeat colics. Jaundiced	1 day	o	++++	Flat plate neg.	E	C	Narrowed	Normal	3	o
53285	Entered in severe colic, operation 3 days later	2 days	+	+	Non vis.	E	C	P	Very small thick fibrin	3	13 chol. 1 ca rim (duct)
38764	Active severe colic	2 days			NV	E	C	P	Adhesions marked, mass perforation	3	20 pigment chol.
30214	Many colics, marked indigestion	Few days	o	o	Non vis. Ca stone	E	P	P	—	2	1
67707	Almost constant R.U.Q. pain, indigestion	Recent	o	o	Non vis.	E	C	P	Distended thickened	3	4 chol. pigment
32302	Entered in acute severe febrile attack	5 days	5 days	?		E	C	P	Very thick, white, tense	3	3 mixed chol. Ca pigment No rings
61348	Several typical colics	Old	o	o	Flat plate neg.	E	P	P	Large thick	2	2 pigment chol.
54973	Emergency septic case operation at once	Active	+	o	Flat plate neg.	E	?	P	Enormous thick white fibrin	3	17 chol., few ca rings
53562	Many typical colics	Few days	o	o	NV many chol. stones	E	P	P	Normal adhesions	N-1	53 chol.
38517	Frequent severe colics	8 days	o	o	Large chol. stone, ca rim, NV	E	Dilated	Large	Thick, adherent	3	1 large chol. Ca rays throughout, ca rim side opposite surface
12869	25 colics, much indigestion	Active	o	o	NV large chol. stone	E	P?	P	Normal	2	1 mixed, ca rays throughout, slight ca rim
35576	Ulcer syndrome very tender G.B. 1 colic	Recent	o	o	Non-Vis. Ca stones	E	C	P	Thick	2	Many large faceted chol. with ca rims
20148	2 severe febrile attacks	5 days	4 days	?		E	C	P	Enormous white fibrin thick	3	251 chol.
49188	Repeated febrile attacks	2 days	+		Non vis.	E Drainage of common through cystic	C	P	Very thick tense adhesions white	3	75-80 chol. with some ca rims
66724	2 acute attacks Charcot	5 days	4 days	2 days	Non vis.	E	P?	P	Small thick	3	42 chol.
57934	Severe colic. Still very tender	2 weeks	?	2 weeks	Non vis. 1 ca stone	E	C	P	Thick œdema fibrin	3	17 mixed ca
69793	Many colics. Entered acute stage	1 day	o	o		E	P	P	Moderately thick distended	2	15 chol. Slight ca rings
55250	Many severe colics. Entered active, remained tender	3 days	o	o	NV many chol. stones	E	P	P	Slightly thickened few recent adhesions	1	244 chol.

See Footnotes for Table I.

TABLE II.—ACUTE

Bile								Sediment		Total in G.B.		G.B. Wall		Cultures		P.O. Reaction
c.cm.	W.B.C.	B.S.	Chol.	BS/Chol.	Ca	CO_2	pH	Chol.	Ca	Chol.	Ca	Chol.	Ca	Wall	Bile	
12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
8		873.1	300	3												o
10	6800	72	8.1	9		35.5	6.84	.758		1		360	45	B. coli	B. coli 5,000,000	o
6		o	31.2	o						1.86						o
5.5	4250	o	68	o	90	17.5	6.0	.025	.002	3.64	4.5	o	105	Staph. B. coli	Staph. diphtheroids, B. coli innumerable	o
19		o	15	o	12	20	6.8			3.00				Staph. A	Staph. A	o
														S	S	o
2.5	3240	610.6	300	2	11.3					7		1410	640	S	S	o
2.5	1250	182	395	.5	10.8					10	.28	1500	720	S	S	o
15	875	o	82	o	7	32	7.24			12	.9	230	110	B. welchi	B. welchi 25	o
37	1026	450	9	50	13.7	77.1	7.61			14.67	2.22			S	Staph. A 100	o
2.5	1250	1399	384	4	20.8			o	o	8.6	6.52			S	S	Sl
		622	38	16						4.37				S	S	o
7		45	360	.12						25.2				S	S	o
8		272	138	2	15.5					11.04	1.24			S	S	
75	11000	o	Slight trace	o	10.7	28.7		.60	2.4			375	110	B. coli	B. coli innumerable	++ abscess
1.5	1760	329	500 with crystals	.6						.75		855	130	Strep.	Strep.	o
0.5		o Qual	+ Qual	o								2100	190	Staph. A	Staph. A	o
10														B. coli +++	B. coli	o
2.5	4400	2605	150	17	30	50		1.5		61.5	12	496	240	S	S	o
13	4212	2871	102	28	30.1	29.9	6.99	.0027		2.86	3.90					o

TABLE III.—CHRONIC

Case No.	Type	Last colic	Last fever	Last jaundice	X-ray	Operation	Gross pathology			Sections	Calculi
							Cystic	Common	Gall bladder		
	1	2	3	4	5	6	7	8	9	10	11
24799	Colic, heart burn	2 weeks	0	0	NV. Chol. stone	E	P	P	Slightly thickened	N-1	2 chol. pigment
53408	Colics, fever	5 days	?	0	Non vis.	E	?	P	Small, greatly thickened	N-1	1 mixed Ca, no rim
37712	Colics, indigestion, once jaundiced	2 days	0	+ old	NV. Large Ca stone	E	Partly C	P	Normal	2	3 chol. pigment. Ca on near duct
55878	Colics, jaundice, cirrhosis	Old	0	+?	Non vis. *Kalkmilchgalle*	E	C	P	Large, thick, adherent cirrhosis	1	3 *Kalkmilchgalle*. 1 mixed Ca no rim 2 chol.
41688	Febrile colics, indigestion	2 weeks	Charcot?	0	Non vis. Ca stone	E	P	C	Dilated	1?	15 chol. with Ca in fractures. Large stone heavy Ca rim
55969	Short sharp colics after meals	0	0	? old	Non vis.	E	P	P	Distended	1	5 chol. Ca rims ++
55901	Many febrile attacks	Old	0	++ old	NV. Ca stones	E	P	P	Slightly thickened	N	10 Ca pigment burr type
36225	Colitis with mild colics?	5 days	0	2 weeks	Non vis.	E	C	P	Subacutely inflamed, thickened	1	5–6 chol.
28053	Chronic R.U.Q. pain, mild colics?	0	0	0	Non vis. Ca stone	E	C	P	Thin and tense, stone in duct	1–2	1 $CaCO_3$
67657	Severe colics with deep jaundice	4 days	0	few days	NV	E	P	P	Large, white, tense	N	100 chol.
20325	Severe colics	2 weeks	?	0	Non vis. Calcification	E	C	P	Flaccid, thickened	2	3–4 chol. stone in Ca milk
32971	Colics, indigestion	0	0	0	N. Flat plate	E	P	P	Normal	N-1	2 chol. Ca ring
46935	Colics, indigestion	Old	0	0	Non vis. Ca stone	E	C?	P	Normal	?	1 mixed stone. Ca on one side
37124	Active afebrile colics	0	0	0	Non vis. Ca mass	E	C	P	Small, tense adhesions	1	Small chol. Ca rim *Kalkmilchgalle*
34902	Colics, chills fever	2 days	?	0	NV. Many chol. stones	E	P	P	Thick adhesions	1	20 chol.
35861	Atypical R.U.Q. crises	Recent	Old	0	NV. Many chol. stones	E	P	P	Thick	2	4 chol. pigment
33293	Colics, indigestion	3 weeks	0	0	Non vis. 1 large stone	E	C	P	Large, thick	3	Chol. 1 pig. $CaCO_3$
37847	Colics, jaundice, mass	2 weeks	0	+	Non vis.	E	C	P	Adhesions, hydrops	2	7–3 chol. 4 Ca pig. no rings
51490	Colitis and non-visualization	Old	0	0	Non vis.	E	?	P	Normal	1–2	845 chol., few Ca rims
53839	Many afebrile colics	1 day	0	0	Non vis.	E	P	P	Large, white, and thick	1	81 chol.
20044	Chronic indigestion, one afebrile colic	Few days	0	0	Non vis. Large Ca stone	E	C	P	Small, thick, collapsed	N	2 *Kalkmilchgalle* Ca rim, 1 duct stone
6584	Many colics, G.B.?	Old	0	0	NV. Large Ca stone	E	P?	P	Normal	N or 1	1 large dotted Ca no rim
55251	Severe colics	1 month	0	1 month	Non vis. Many Ca stones	E	C	P	White, thick, hard	2	6 diffuse Ca no rings
26206	No G.B. symptoms, operated on, X-ray	0	0	0	Ca stone NV	E	P	P	Normal	N	1 Ca pigment
48677	Severe colics with jaundice	Old	Old	Old	Non vis.	E Stones in common duct	Dilated	C partly	Slightly thickened	2	6 chol. pigment

See Footnotes for Table I.

TABLE III.—CHRONIC

Bile								Sediment		Total in G.B.		G.B. wall		Cultures		P.O. Reaction
c.cm.	W.B.C.	B.S.	Chol.	BS/Chol.	Ca	CO_2	pH	Chol.	Ca	Chol.	Ca	Chol.	Ca	Wall	Bile	
12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
		o	831		40	32	6.96							S	S	o
o		o	+	o												o
19		344	128	3						24.32						
		o qual.	+ qual.	+	kmg									S	S	o
8		1577	36	44						2.88				S	S	o
35	2176	1267	98	13	38	33.2	6.6			33	12	520	778	B. coli	B. coli innumerable	o
22	450	6151	375	16	42	24	7.06	.37		83	9	320	1000	S	S	o
9	1150	o	33	o		17	6.5			3		3640	170	B. typhosus	S	o
	few	o	o	o	10.6	11.2	6.82							S	S	+
18	550	3712	114	33	41	30	6.91	1.55		21.9	7.3	1080	680	Staph. aureus	S	o
		o qual.	+ qual.		kmg						kmg			S	S	o
23		1302	138	9	319					31.74	7.36			S	S	o
		o			15.4	29.5	6.8							S	S	o
		o			14.5 kmg	14.1					kmg			S	S	o
		1310	188	7										S	S	o
		735	96	8										B. coli	B. coli	++
18		o	114 with crystals	o	10.1	6.6								S	S	o
		o			10.3	6.6										
		o	282 with crystals	o	562.8									S	S	o
1		o	500 with crystals	o						5		405	120	Green strep. staph.	B. welchi	o
16	3460	1375	73	19	44	47.7	7.2	2.8	.015	9.85	10	294	243	S	S	o
		o	o	o	103	55	7.2				kmg			S	S	o
6	2460	1524	44	35	87	49	6.81	o	o	2.62	5.22	800	6400	Staph. B. welchi	Strep. 50	o
26	3124	o	9	o	12.3	11.6	6.8	.025		2.67	3.12			S	Few staph.	o
					31.2	84.1	7.22									o
2		269	500 with crystals	.5						.10		375	140	B. coli	B. coli, many	

TABLE IV.—BACTERIAL FINDINGS IN DIFFERENT TYPES OF GALL BLADDERS

	Sterile	Infected*
Normal	3	3
Normal with stones	3	1
Jaundice	3	0
Acute	7	10
Chronic	14	8

*If bacteria are found in either bile or gall-bladder wall.

TABLE V.—BACTERIAL FINDINGS IN RELATION TO CYSTIC DUCT PATENCY

	Sterile	Infected*
Duct open		
Acute	4	3
Chronic	6	2
Duct closed		
Acute	3	8
Chronic	9	1

*If bacteria are found in either bile or gall-bladder wall.

5. *Chronic cases* (Table III). In this case all had stones and most but not all had definite pathological findings in the gall bladders, and had definite histories of undoubted attacks of biliary disease.

Microscopic studies. These are being reported in detail in another paper, but a short summary of the findings thus far will be given here. The first observation was the decided difference with which the tissue behaved when put into fixatives. In many cases a gall bladder which had seemed thickened in the fresh specimen, failed to contract in formalin. Others that were quite thin in the fresh specimen contracted to such an extent that in section they appeared very thick. This lack of correlation was so striking that at first it was thought that specimens might have been mislabeled. No reason for this has been found so far. Second, the mucosa, in the great majority of cases was surprisingly normal, even in the acute cases. By the technique described it at once becomes evident that the mucosa is well preserved in most cases, and the villi are intact. Third, the severity of the inflammatory changes is greatest nearly always in the serosa. In other words the inflammation seems to reach the gall bladder from without and not from the bile. This was suggested by us in a previous article (4). Fourth, the degree of inflammatory changes discovered histologically, is not commensurate with the symptoms produced, and the walls of these gall bladders are not comparable with the walls of other inflamed viscera, such as the appendix or urinary bladder. In other words, the changes found are quite possibly due in the vast majority of cases to obstruction or some such factor and not to infection *per se.*

Cultures (Tables I–III, columns 26–27). In view of the elaborate nature of the technique followed, the small number of bacteria found in most cases has been surprising. In 25 cases both gall-bladder wall and bile were sterile, and in 28 one or the other contained organisms. Biliary tract infection did not seem to be significantly higher in any one group of the classification than the other (Table IV). Thus, while half of the normals contained bacteria, actually less than half of the entire infected group did. On the other hand, the finding of bacteria was about twice as common in the acute 59 per cent as in the common cases, 28 per cent. If these statistics are re-arranged according to whether or not the cystic duct was patent, an interesting fact is seen (Table V). If the duct is patent, there is no significant difference between the acute and chronic cases, but if the cystic duct is closed, the acute cases gave bacterial growth in 8 of 11 cases but in the chronic group it was sterile in 9 out of 10 cases. This agrees well with our previously reported experiences in animals (4) that closure of the cystic duct brings about an infection of the gall bladder, and that eventually the organ sterilizes itself and lies as a functionless viscus, without causing harm unless reinfection occurs.

The route through which the infection occurs also is shown. There were 7 cases in which the gall-bladder wall contained bacteria and the bile was sterile. This contrasts sharply with only two in which the wall was sterile and the bile contained organisms. In these 2 cases only small numbers of staphylococci were present in the bile. Throughout the entire series the organisms found in the bile were very few in numbers, compared to the rich growth often found in the wall. When one considers the facts brought out by Arnold, as to the enormous number of bacteria which pass out of the digestive tract into the lymph stream and the finding of a rich flora in the normal liver reported in our studies on liver autolysis (3, 8), one cannot help feeling that these organisms represent the normal flora of the

region derived from the gastro-intestinal tract. This is further borne out by the wide variety of bacteria found: Bacillus welchii, streptococci of several kinds, including fæcalis alkaligenes; Staphylococci, albus, aureus, and a hæmolytic type; Diphtheroids; and Bacillus Typhosus. Our results then indicate that infection reaches the gall bladder from without and not from within, and correspond well with the microscopic studies.

The colon bacillus appears to be a striking exception to these statements. In the first place, when present at all, it generally can be recovered in enormous numbers. Instead of ranging from a few to 100 per cubic centimeter, it is usually over five million per cubic centimeter which was about the limit of possible counts by the dilutions used in making the plates. Its association with the more severe cases was quite unusual. It was found in 9 cases. In 3 the patients died; a fourth patient developed a large postoperative abscess in the gall-bladder bed; in the fifth, profuse wound suppuration occurred resulting in a hernia; in the sixth, the patient had a fever to 105 degrees following cholecystectomy. The seventh patient nearly died of paralytic ileus and enormous distention. Of the 2 remaining cases 1 had only a few organisms per cubic centimeter of bile. From these figures then it seems that the colon bacillus was associated with most of the postoperative disasters in the entire series reported, and its presence is of grave prognostic significance, it being the only organism which appears in enormous numbers in the bile. In this series there was no case of really totally gangrenous gall bladder, and the Welch bacilli were not found in large numbers in any culture. Their presence in small numbers did not seem to have any prognostic significance. They appear simply to represent portions of the normal liver flora. Our previous finding of these organisms in gangrenous gall bladders is probably explained on this basis, and we no longer regard it to be of grave significance.

Pus in the bile. In such a short series there were naturally but few cases of empyema of the gall bladder. However, when apparently found, we were surprised to find that the diagnosis would not stand up under more detailed analysis. When smears and white counts were made, the "pus" resolved itself into a mixture of débris made up of small cholesterol crystals, fine amorphous cholesterol in suspension, calcium, and pigment débris. This is shown very clearly in the white blood counts made in the bile. A study of these counts (column 13 in Tables I–III) shows at once that pus is not found in the bile. In the acute or chronically infected cases no more than the normal wandering cells were shown and no relation could be made out between this and any other factor. In several of the severely infected cases the count was actually lower than normal. Again a striking exception is one of the Bacillus coli cases, which developed a postoperative abscess. It was the only one in the entire series with a significant elevation of the white count. These results also militate strongly against any theory of biliary origin to gall-bladder disease.

TABLE VI.—BILE SALTS AND CHOLESTEROL IN DIFFERENT TYPES OF GALL BLADDERS

	Bile salts	Cholesterol	B.S.-Chol. Ratio*
Normal	3342	158	21
Normal with stones	1772	129	14
Jaundice	2089	157	13
Acute	568	178	3
Chronic	811	144	5

*Ratio figured from averages of bile salts and cholesterol, not average of individual ratios.

Bile salts and cholesterol. The findings in this series agree closely with our previously reported animal experiments. A summary of the data is given in Table VI. The following points are to be especially noted:

a. The bile in normal gall bladders without stone contains about 20 times as much bile salts as cholesterol, amply sufficient to hold the latter in solution and thus prevent stone formation. In the case of normal gall bladders containing stones the ratio is slightly lower, about 14 and quite near the critical level for precipitation. Here, as in many of the later classifications, isolated cases may be found by consulting the large tables (I–V) where cholesterol stones are found in bile far below the saturation point. This emphasizes the well known fact that even cholesterol stones are not soluble in human bile to any appreciable extent. As we previously showed the cholesterol is in a chemical combination with the bile acids, and its precipitation is an irreversible

TABLE VII.—RELATION OF BILE SALT ABSORPTION TO CYSTIC DUCT CLOSURE

Duct patent			Duct closed		
B.S.	Chol.	Ratio*	B.S.	Chol.	Ratio*
1399	384	4	0	68	0
622	38	16	873	300	3
2605	150	17	72	8	9
1577	36	44	0	31	0
1267	98	13	610	30	2
6151	375	16	182	394	0.5
3712	114	33	212	138	1.5
1302	138	9	0	—	0
1310	188	7	329	500	0.6
735	96	8	344	128	2
1375	73	19	0	—	0
1524	44	35	0	33	0
			0	0	0
			0	114	0
			0	282	0
			0	0	0
			0	9	0
Aver.— 1988	136	15	152	144	1

*Ratio figured from averages of bile salts and cholesterol, not from individual averages.

change, i.e., the breaking up of a chemical compound (9).

b. In the cases with jaundice the ratio is within the normal range. Thus no evidence is seen that stasis alone is a factor. If it were one would expect that in common duct obstruction the bile stagnant in the gall bladder would undergo changes similar to those reported in the series of acute and chronic types. Other writers have claimed that in these cases there was an accumulation of cholesterol in the gall bladder due to excretion by the mucosa. This phenomenon certainly does not appear in our analyses, or in the other cases of partial obstruction of the common duct classed in the other series. Previous dog experiments on 78 dogs, in about half of which the common duct had been ligated, had also failed to reveal any accumulation of cholesterol in the gall bladder (16).

c. In the acute and chronic types there is a marked evidence of absorption of bile salts at the expense of the cholesterol. The former are sharply reduced in most cases and often completely absorbed. The cholesterol content does not rise, but remains usually within normal limits. When the bile salts are absorbed it is precipitated and found in the sediment, either crystalline or amorphous. The average in the chronic type is to find about five times as much bile salt as cholesterol and in the acute about three times as much. When one considers that most diseased gall bladders contain far less bile than normal ones, the claim of Naunyn and more recently Elman and Graham that cholesterol is excreted into the gall bladder by its mucosa receives no substantiation. In spite of the fact that the total bile is lessened, the cholesterol concentration is low or normal. This can be seen in the big tables (I–III, columns 14–16). The total cholesterol in the gall bladder, far from being raised, is markedly lowered in the pathological cases and it is clear that it is not only not secreted but in the presence of prolonged cystic duct obstruction is gradually absorbed. This apparently takes place after precipitation when the small particles are taken up by wandering cells.

Importance of cystic duct obstruction. The intentional vagueness in the use of the term diseased gall bladder may be somewhat cleared up if the figures for bile salts and cholesterol in Tables II and III are studied in relation to cystic duct obstruction. A glance at these tables shows at once that, although the averages of the series are lowered, figures of all sorts are found, from zero up to normal levels. If, however, the cases of cystic duct obstruction are put into one column and those with patent ducts into another (Table VII), a very clear correlation is at once evident. Those with closed cystic ducts have a ratio of about one while those with open ducts have normal ratios. Much more important, the findings are quite regular, *all* the patent ducts give comparatively normal ratios and *all* the closed ones show a rapid absorption of bile acids and a much slower absorption of cholesterol.

Sediment in the bile (Tables I–III, columns 20–21). When the specimen was large enough after centrifuging, the sediment was analyzed separately. The figures given must be considered only approximate as the separa-

tion of precipitated substances from bile is very difficult. Amorphous cholesterol is often in such a fine state of dispersion that it will pass through filter papers. Centrifuging is the method of choice and usually yielded perfectly clear supernatant fluids. The striking fact elicited from these studies was the very small amount of cholesterol found in any of the sediments. It was so little as to be insignificant in every case, the highest figure being under 3 milligrams, in most cases being under 1 milligram, although the total amount of the sediment might be considerable. This seems to indicate that cholesterol stones are formed and grow by actual crystallization of cholesterol on nuclei or stones and not by agglomeration of amorphous sediment into masses. Such finely divided cholesterol is probably carried out through the cystic duct if it is open and, if not, is removed by wandering cells.

The same is true although in a lesser degree of calcium. It is not found often in large amounts in the sediment, except in the cases of *Kalkmilchgalle*. In other words it seems that the calcium is precipitated directly onto stones and not molded onto them from the sediment.

The sediment consists of a mixture of organic compounds, proteins and their derivatives, fatty acid, fats, and contains a minimum of stone forming substances, except pigment which is often found in considerable quantities.

Total quantities in the gall bladder. These are given in columns 22–23 in Tables I–III. It is evident that in general the normal gall bladders contained the most material. If these figures are studied in relation to the patency of the cystic duct, it becomes quite clear that the function of the closed viscus is an absorptive and not a secreting one. Much less cholesterol is found in closed gall bladders, and as has been before stated the bile salts are rapidly absorbed.

The conspicuous exception is calcium which as has been shown by Phemister and by ourselves is excreted by the gall-bladder mucosa.

Calcium. Wilkie has reported the finding of calcium gall stones in animals after bacterial injection and cystic duct ligation. Phemister (24) successfully repeated these experiments and called attention to the fact that in the clinic calcium gall stones were definitely associated with cystic duct closure. Our own experiments showed that infection was not necessarily a factor, first as calcium was rapidly absorbed from the acutely infected gall bladder (5), and second because this calcium excretion was experimentally reproduced without infection (2). The analyses in this series confirm these findings. Table VII shows that the bile entering the gall bladder is not a significant factor as its calcium content is not changed appreciably from the normal in diseased cases. In a recent paper (5) a series of 45 calcium estimations on dog bile gave results which are almost identical with those in Table VIII. It appears then that, during the early stages of obstruction and consequent infection, the gall bladder absorbs not secretes calcium, but later after conditions have become quiescent, a distinct excretion occurs. Reference to the large tables (I–III), however, shows that if the duct is closed the calcium in solution (column 17) is small in amount in the acute cases but in the chronic or quiescent cases it tends to run higher or even produce *Kalkmilchgalle*.

TABLE VIII.—CALCIUM IN THE BILE

Normal (6 cases)	33
Normal with stones (4 cases)	17
Acute (10 cases)	26
Chronic (13 cases)	26

Figures in mg. per cent.

Reaction of bile (Tables I–III, columns 18–19). The hydrogen concentration of the bile or gall-bladder contents varied only in a narrow range and these changes did not seem to bear any relation to any other factors in these studies. They were far less than the changes in reaction reported by Rous between liver bile and bladder bile, and no conclusions can be drawn, except that our work does not show that the hydrogen-ion concentration bears any relation to gall-bladder disease. The carbon dioxide combining power (Van Slyke) also gave results from which no conclusions may be drawn. It varied over an exceedingly wide range, and could not be shown to bear any relation to the hydrogen-ion concentration, the chemical content of the bile, or the condition of the gall bladder.

Gall-bladder wall (Tables I–III, columns 24–25). The enormous variations in the content

of the gall-bladder wall in cholesterol and calcium are striking, but appear to follow no consistent rule that we can make out. The fluctuations are so great that it seems a logical deduction that either excretion or absorption is going on but in which direction the flow is cannot be ascertained. Especially disappointing has been the attempt to correlate the histological picture with the chemical one. This has been due perhaps to the fact that in strawberry gall bladders, the deposits tend to be local and a section of one part and chemical analysis of another would naturally yield discordant results. In work under way now, attempts are being made to correct this.

DEDUCTIONS

Considering the data enumerated together with our recent experimental studies, it is possible to build up a fairly comprehensive, although tentative, theory as to the origin and progress of gall-bladder disease.

1. To the perennial question as to whether the infection precedes the stone or vice versa, the answer may be given that the evidence is in favor of the infection being the causative agent. After considerable experimental work as well as clinical studies, no evidence is forthcoming that the liver ever secretes bile at the saturation point (7, 13). There is no evidence that gall stones *per se* are associated with hypercholesterolæmia, or even that hypercholesterolæmia will cause an increased amount of sterols in the bile. Finally a definite mechanism has been demonstrated by which infection will cause stones (9).

2. The possible routes for this infection are three, hæmatogenous, chologenous, and by direct extension from the liver. In animal experiments most enormous doses of bacteria intravenously are needed to cause a cholecystitis, far more than ever happens clinically. As to a biliary origin, although numerous authors report the passage of injected bacteria into the bile, again the doses used are beyond reason. Graham has shown that the liver acts as a rather efficient filter and will hold back injected bacteria in amounts that exceed those found in human blood except in most severe bacteriæmia. On the other hand, the rich flora of the liver affords an obvious and simple explanation. Dragstedt (14) showed that the Welch bacillus was a constant inhabitant of the normal liver. Our own work has confirmed this and also demonstrated that this viscus contained most of the intestinal flora in considerable numbers. The prompt infection of a dog's stasic gall bladder with this flora is easily demonstrated (4). The observations reported in this paper lend strong support to the view that the liver is the source of the infection. In the few cases in which high bacterial counts as well as the stormy course indicate marked infective process, the colon bacillus was the offending agent and it seems reasonable to assume that it is the actual cause of the first cholecystitis which causes stone formation.

3. Sections through the cystic duct and the lower end of the gall bladder show a surprisingly complex arrangement of valves and folds. This is so marked as to lead some observers to question whether the gall bladder can ever empty itself. It is quite clear that the least swelling or œdema in this region would promptly close off the duct. After the first small stones have been formed, it may then act as a stopper in subsequent attacks and cause stasis, either temporary or permanent. The overwhelming majority of our cases which showed pathological change had stones and besides the paucity of bacteria, even in the acute ones, indicates that mechanical obstruction is the important element in most attacks, and only rarely will a patient be operated upon in the first attack in which the bacteria are the offending agents.

4. The train of events being thus initiated, each subsequent stoppage of the duct with resulting infection, brings about further absorption of bile acids with further deposits of cholesterol on the stones. If the stasis is of short duration, as is usually the case, the deposit is cholesterol. If it is prolonged, the infection tends to clear up, as we have shown in animal experiments, and the secretion of calcium from the gall-bladder wall results in calcium rings about the stones or in fractures in the stones. A resolution and recurrence of short septic attacks may thus result in alternate layers of calcium and cholesterol. Com-

plete, permanent stoppage results in *Kalkmilchgalle* or pure calcium stones.

5. Pigment studies are handicapped by lack of suitable microchemical methods. However, the following facts are clear. Pigment is not precipitated as a simple calcium salt, the amount of calcium being far too great for this. Cholesterol stones seldom have pigment nuclei. Pigment is usually associated with calcium in gall stones. Pigment stones may result from supersaturation as in hæmolytic jaundice, and in the common bovine gall stones. These stones form readily in experimental animals in any condition characterized by inspissation of the bile; they even form in the dilated ducts of dogs with common duct ligation. All that one can say of them is that under condition of concentration, increased excretion with perhaps the factor of changing reaction of the bile, pigment may be precipitated. This is deposited in amorphous masses in and about gall stones, and under rare conditions may be precipitated in a pure state.

The question of chemical cholecystitis. Several points in our work might easily lead to the interpretation that cholecystitis is not a bacterial disease. These points are, the many sterile gall bladders found in acute cases, the low white counts in the bile, and the lack in many cases of the microscopic picture of an acute infection.

There are other facts available which point in the same direction. First, there is the experimental method of producing gall-bladder inflammation in dogs by the intravenous injection of Dakin's solution (21). Second is the demonstration by Wolfer that pancreatic juice will provoke a cholecystitis. This has been confirmed in our laboratory (1). Third, the report by Judd (23) of numerous cases of apparently acute cholecystitis which yielded sterile cultures.

Therefore with these several points in mind it is very difficult to deny the possibility of the entrance of a sterile irritant, such as pancreatic juice, even duodenal content into the gall bladder. Excretion by the liver of bile containing chemical irritants is also a possibility. The answer to these questions must await more careful chemical analysis of bile from acute cases.

BIBLIOGRAPHY

1. Andrews, E., Dostal, L. E., Goff, M., and Hrdina, L. Mechanism of cholesterol gallstone formation. Ann. Surg., 1932, xcvi, 615.
2. Andrews, E., Dostal, L. E., and Hrdina, L. Etiology of gallstones. IV. Is cholesterol excreted by the gall-bladder mucosa? Arch. Surg. (awaiting publication).
3. Andrews, E., and Hrdina, L. Cause of death in liver autolysis. Surg., Gynec. & Obst., 1931, lii, 61.
4. Andrews, E., and Hrdina, L. Hepatogenous cholecystitis. Arch. Surg., 1931, xxiii, 201.
5. Andrews, E., and Hrdina, L. Absorption of calcium from the gall-bladder. Am. J. Med. Sc., 1931, clxxxi, 478.
6. Andrews, E., and Hrdina, L. A method for estimation of both bile salts and cholesterol in small amounts of bile. Proc. Soc. Exper. Biol. & Med., 1932, xxxix, 1102.
7. Andrews, E., Hrdina, L., and Dostal, L. E. Etiology of gallstones. II. Analyses of duct bile from diseased livers. Arch. Surg. (awaiting publication).
8. Andrews, E., Rewbridge, A. G., and Hrdina, L. Causation of B. Welchii infections in dogs by injection of sterile liver extracts or bile salts. Surg., Gynec. & Obst., 1931, liii, 176.
9. Andrews, E., Schoenheimer, R., and Hrdina, L. Etiology of gallstones. I. Chemical factor. Arch. Surg., 1932, xxv, 796.
10. Arnold, L. Alterations in the endogenous bacterial flora and microbic permeability of the intestinal wall. J. Hyg., 1929, xxix, 82.
11. Bloor, W. R. The determination of cholesterol in blood. J. Biol. Chem., 1916, xxiv, 227.
12. Clark, E. P., and Collip, J. B. A study of the Tisdall method for the determination of blood serum calcium with a suggested modification. J. Biol. Chem., 1925, lxiii, 461.
13. Dostal, L. E., and Andrews, E. Etiology of gallstones. III. Variations of the bile salt-cholesterol ratio under dietary influences. Arch. Surg. (awaiting publication).
14. Ellis, J. C., and Dragstedt, L. R. Liver autolysis *in vivo*. Arch. Surg., 1930, xx, 8.
15. Elman, P., and Graham, E. The pathogenesis of strawberry gall bladder. Arch. Surg., 1932, xiv, 24.
16. Goff, M., Hrdina, L., and Andrews, E. Effect of prolonged stasis on the bile salt-cholesterol ratio. Proc. Soc. Exper. Biol. & Med., 1932, xxix, 549.
17. Graham, E. A., and Peterman, M. G. Further observations on lymphatic origin of cholecystitis. Arch. Surg., 1932, iv, 23.
18. Hastings, A. B., and Sendroy, J., Jr. Studies of acidosis XX. The colorimetric determination of blood pH at body temperature without buffer standards. J. Biol. Chem., 1924, lix, 695.
19. Koch, F. C. A modified Van Slyke amino-nitrogen apparatus. J. Biol. Chem., 1929, lxxxix, 601.
20. Kramer, B., and Tisdall, F. F. A simple technique for the determination of calcium and magnesium in small amounts of serum. J. Biol. Chem., 1921, xlvii, 475.
21. Mann, F. C. Production of chemical cholecystitis. Ann. Surg., 1921, lxxiii, 54.
22. Naunyn, B. Cholelithiasis. Leipzig, 1892.
23. Nickel, A. C., and Judd, E. S. Cholecystitis: A bacteriological and experimental study of 300 surgically resected gall bladders. Surg., Gynec. & Obst., 1930, l, 655.

24. PHEMISTER, D. B., REWBRIDGE, A. G., and RUDISILL, H. Calcium carbonate gallstones and calcification of the gall-bladder following cystic-duct obstruction. Ann. Surg., 1931, xciv, 493.
25. PHEMISTER, D. B., DAY, LOIS, and HASTINGS, A. B. Calcium carbonate gallstones and their experimental production. Ann. Surg., 1932, xcvi, 595.
26. SCHMIDT, C. L. A., and DART, A. E. The estimation of bile acids in the bile. J. Biol. Chem., 1920, xlv, 415.
27. VAN SLYKE, D. D. The quantitative determination of aliphatic amino groups. J. Biol. Chem., 1912, xii, 275.
28. VAN SLYKE, D. D., and MCNEILL, J. The determination of gases in blood and other solutions by vacuum extraction and manometric measurement. J. Biol. Chem., 1924, lix, 523.
29. WILKIE, A. L. Bacteriology of cholecystitis. Brit. J. Surg., 1928, xv, 450.
30. WOLFER, J. A. The rôle of the pancreatic juice in the production of gall-bladder disease. Surg., Gynec. & Obst., 1931, liii, 433.

PARAVERTEBRAL ANÆSTHESIA IN OBSTETRICS

Experimental and Clinical Basis[1]

J. G. P. CLELAND, M.Sc., M.D., C.M., F.A.C.S., Oregon City, Oregon
From the Department of Physiology, University of Oregon, and The Oregon City Hospital.

PAIN in labor, in spite of the remarkable advances in anæsthesia during the past quarter of a century, still remains a necessary concomitant of normal delivery. There seem to be two valid reasons for this: first, the disadvantages of general anæsthesia and/or narcosis are enhanced in obstetrics by the peculiarly long period of administration, producing toxic effects on the child, the mother, or the uterus itself, which contra-indicate adequate dosage; second, the lack of definite knowledge concerning the paths of afferent nerves of the uterus to the cord, has prevented the scientific application of regional anæsthesia.

Regional anæsthesia, so successfully developed in other fields of surgery, should find its ideal application in obstetrics, if a method were developed whereby the sensory nerves could be blocked without appreciably affecting the motor nerves of the uterus. In this field, spinal anæsthesia not only lacks the safety of other forms of regional block, but also impairs the expulsive power of the uterus; whereas, caudal block does not relieve the pain of uterine contraction. Paravertebral block of nerve roots has not apparently been tried owing to the large number of them attributed to the uterus by clinical observations of areas of hyperæsthesia.

The purpose of this paper is to survey the present status of our knowledge of uterine afferent nerves, to present experimental proof *via* visceromotor reflexes of the location of these paths in the dog, to correlate these findings in man, to explain the error of conclusions hitherto accepted, and to demonstrate that the pain of uterine contraction may be abolished without affecting the contractions by paravertebral block of only two adjacent nerves.

PRESENT STATUS OF KNOWLEDGE OF AFFERENT NERVES OF THE UTERUS

Much conflicting evidence has been published on the afferent supply of the uterus. Behan considered these fibers to be of cerebrospinal rather than sympathetic origin, that they come from the second, third, and fourth sacrals or the third and fourth sacrals—and that it is due to stretching of these nerves that pain is felt in labor. Nevertheless, experiments of caudal anæsthesia in labor at the Royal Victoria Maternity Hospital, Montreal, in 1927, demonstrated that although relaxation and insensitivity of the perineum and adjacent parts indicated that the sacral nerves had been successfully blocked, the labor pains were undiminished. These experiments are in accord with the salient fact discovered by Cotte, 1925, that all pain of uterine contraction, in dysmenorrhœa, is abolished by section of the superior hypogastric plexus. Leriche and Stricker, 1927, demonstrated the presence of sensory fibers in this plexus; and Fontaine and Hermann, 1932, proved that dysmenorrhœa and other forms of severe pelvic pain may be consistently relieved by its section as high as the inferior mesenteric ganglion: but its position on the anterior aspect of the aorta makes it too inaccessible for practical regional block. It is necessary, therefore, to trace the uterine afferents to the nerve roots.

Evidence on the afferent connections of the uterus with the cord, by clinical observation of areas of hyperalgesia, is contradictory and inconclusive. Head found the pain of labor to be associated with tenderness over the eleventh thoracic segment definitely, often the twelfth, too, sometimes the tenth and occasionally the first lumbar; and the after-pains to be associated with the third sacral, as well as all these. MacKenzie observed that pain is felt between the umbilicus and pubis, across the back at the level of the top of the sacrum, and rarely referred to a lower level, but that it may extend from the tenth thoracic to the third lumbar nerves. Pottenger, while admitting that clinical observation of pain and sensation must of necessity be more or less uncertain,

[1]These investigations were begun at McGill University, 1927, and carried to completion at the University of Oregon, Department of Physiology, with the co-operation of Professor G. E. Burget 1930-1932. The clinical application was made at the Oregon City Hospital, 1932.

believed that uterine pain may be located anywhere in the areas of the tenth thoracic to the fifth lumbar, or even sacral segments. Head's conclusions are quoted in Cunningham's *Anatomy:* "Clinical observations indicate that afferent impulses reach the central nervous system from the uterus through the posterior roots of the tenth, eleventh, twelfth, thoracic nerves, the first lumbar, and the second, third, and fourth, sacral nerves." Kuntz, in his recent thorough and exhaustive text on the autonomic nervous system, 1929, gave these roots as bearing uterine afferent fibers; for which his reference was Cunningham. Yet, in 1922, Head recognized and explained the variability of these areas of hyperæsthesia, summing up his long unexcelled experience in these words: "Referred pain of visceral origin and the tenderness which accompanies it may be confined to the territory of a few segments only, representing the nerve supply of the affected organ. But in the larger number of cases met with in daily practice this is not the case; if the stimulus is extremely severe—as, for example, during an attack of gall stones or renal colic, the pain may spread widely, even in otherwise normal persons." That this is true of the severe stimulus of labor is supported by the observations of Gertsmann, 1926, when he reported a case of gestation in a woman with a lesion of the cord at the level of the first lumbar vertebra, in which sensory and motor powers of the uterus were retained. He quoted Langley and Anderson in affirming that the sacral nerves did not take part in the innervation of the internal generative organs.

VISCEROMOTOR REFLEXES AS AN INDEX OF AFFERENT NERVES

In 1909, MacKenzie, having demonstrated clinically that abdominal muscles possess the power of contraction in small sections in response to visceral stimulation, coined the phrase "viscero-motor reflex." He considered this to be due to hyperirritability of the spinal cord in the vicinity of the visceral afferent neurones. He concluded that, as the motor supply is better known than the sensory, we might by this means more accurately ascertain the segment of stimulation in the cord. Nevertheless, in the absence of a means of accurately marking out the limits of motor activity, he based his conclusions in regard to the afferent supply of the viscera on sensory disturbances.

A method of recording visceromotor reflexes and of using them as an index of the afferent connections to the cord of any particular viscus, was worked out on the spleen by Cleland and Tait 1926, cats and dogs being used. It was found that widespread synapses occur within the cord from the limited afferent neurones to the extensive efferent neurones of the same organ. Since experience in 1927 with caudal anæsthesia in labor seemed to dispose of the idea of the sacral distribution of uterine afferents as erroneous, it was apparent that the afferent nerves of the uterus must enter the cord higher up—probably within the compass of the visceromotor reflexes.

Owing to the relatively greater number of thoraco-lumbar segments and relatively fewer sacral segments in the dog than in man, the problem of applying uterine afferent findings in the dog (by analogy) to man, would be difficult were it not for the works of Edgeworth and Head. Edgeworth, 1892, found the visceral afferent fibers to enter the cord, in the dog, between the first thoracic and the third lumbar, and between the seventh lumbar and the second sacral, thus leaving a gap of three segments. Head, 1893, found that in the human the distribution of the afferent sympathetic to the cord is between the first thoracic and the first lumbar, and between the fifth lumbar and the fourth sacral, thus leaving a gap of three segments. Since in each case the lower limit of the sympathetic distribution is the next to last sacral, one may, counting from below upward infer that the fourth lumbar in the dog corresponds to the second lumbar in man. Johnston, 1906, found that in all higher classes of vertebrates the arrangement of the spinal nerve roots along the trunk is the same. The relationship of afferent and efferent neurones in the cord, according to Pottenger, 1922, is preserved in the process of evolution; and, while some of the viscera are markedly displaced, they still keep their primitive nerve connections. The constancy of the analogy is further substantiated by the works of Bardeen, Ramstrœm, and Sherrington.

POSSIBLE EFFECT OF PARAVERTEBRAL BLOCK

That pain in labor may be relieved by paravertebral block of nerve roots is suggested by Kappis' work on other organs. A comparison of his findings of the afferent roots from particular viscera, with those of Head and others, show them to be much more limited in extent than areas of hyperalgesia have suggested. Nevertheless (perhaps because of the clinical impractibility of blocking the extraordinarily large number of segments attributed to it by areas of hyperalgesia) he did not, apparently, attempt to thus block uterine pain. Swetlow, 1926, relieved angina pectoris, in a case with hyperalgesia of the first and second thoracic segments, by paravertebral injection with novocain of the first and second thoracic roots; whereas Head's area of hyperalgesia for the heart extends from the first to the seventh thoracic.

Gertsmann, 1926, referred to the experiments on animals of Ludwig, Muller, Balint, and Benedict, to show that the primary centers for contraction of the uterus must be situated *outside* the cord, and *in* the sympathetic ganglia of the pelvis. This is borne out by the experiments of Sir James Simpson, 1871, when he found that parturition was normal in sows from which he had removed the thoracic and lumbar cord, except that the last fetus of the litter remained in the vagina. That this was also true of the cat was shown in a similar experiment by Riemann, 1871. Rein, 1882, noted that spontaneous parturition in the rabbit, following the section of all the extrinsic nerves of the uterus, proceeded with abnormal rapidity. Cannon, 1929, reported parturition in a cat 6 weeks after the exclusion of all sympathetic impulses by removal of the sympathetic ganglia; and normal parturition has occurred in patients after resection of the superior hypogastric plexus had been previously performed for the relief of pelvic pain (Fontaine and Hermann). Moreover, Dellepiane and Badino, 1927, skilfully blocked this plexus by deep paravertebral injection, and relieved pain of uterine contraction without obstructing the course of labor. Whitehouse and Featherstone investigated the cause of increased tone and contraction of uterine muscle under spinal anæsthesia and decided that it was due to the effect of paralysis of the lumbar cord on the para-sympathetic, third and fourth lumbar (thus contracting the circular muscle and relaxing the longitudinal or expulsive muscle). They inferred that paralysis of the sympathetic would have the opposite effect. Since it has been shown that the primary centers for uterine contraction lie in or beyond the sympathetic *ganglia*, however, it would appear that the blocking of a limited number of sympathetic *roots* should not interfere with the motor activity of the uterine muscle. Therefore should the uterine afferent sympathetic be found to be more limited segmentally than the uterine efferent sympathetic (as was shown to be the case with the spleen), paravertebral block should relieve the pain of labor without interfering with its normal course.

TECHNICAL DETAILS OF EXPERIMENTS[1]

The animals used for experiment were dogs and cats.

Since it was found that all anæsthetics and narcotics in doses adequate to prevent pain, depress the reflexes, the "spinal animal," with the cord transected just below the foramen magnum, was used. Artificial respiration was supplied by an air pump. To compensate for the fall in temperature normally appearing in the spinal animals, heat was applied by means of an electric reflector.

Stimulation of the visceral organ was effected either by minimal induction shocks through shielded electrodes to the organ, or its nerve, or by dilatation of the organ (with normal salt solution). The latter method was finally chosen as a more physiological one for the uterus. It was effected by means of a pressure bottle and rubber tubing to a Y tube cannula tied in the cervix. As a pressure gauge, a mercury manometer was interpolated, by a T tube connection, between the pressure bottle and the cannula. To produce a sudden intra-uterine pressure, the bottle was elevated to the desired height, and the pressure clamp released; whereas the more usual gradual distention was applied by pumping air into the pressure bottle, by means of a sphygmomanometer bulb.

Changes in muscle tonus were recorded on a revolving smoked drum, by means of a spring lever actuated by a silk thread attached to the cut end of the muscle. The spring was adjusted so as to balance the normal tonus of the muscle; and the direction of the thread was bent, by pulleys, into alinement with muscle fibers. Contraction of the muscle thus produced a downward motion of the lever, against the spring, to be recorded on the drum. A second spring

[1] My thanks are due Dr. G. E. Burget for having provided facilities and help for these experiments, and for his invaluable assistance both with them and this manuscript.

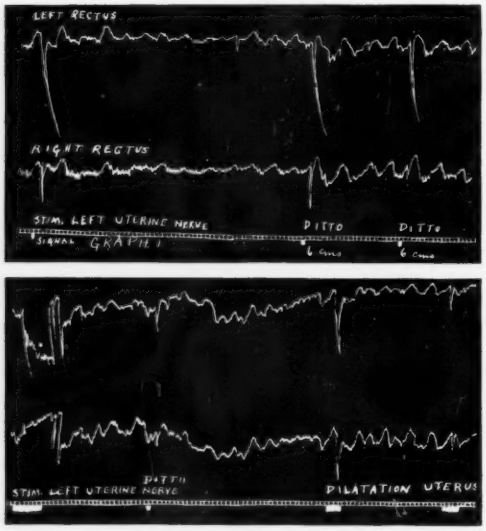


Fig. 1. To show that dilatation of the uterus is an adequate stimulus to its sensory nerves; and also some characteristics of the uterine visceromotor reflex. Contraction of the rectus produces a downward movement of the recording lever. Graph I.

lever was set directly below the other so that changes in tonus of two muscles (usually on opposite sides of the abdomen) could be recorded simultaneously.

The moment of stimulation was recorded by a signal marker on the drum actuated by a key that closed the circuit and produced the stimulation at the same time. A timer recorded two second intervals. The drum was made to revolve at the rate of 1¼ inches per minute.

In order to immobilize the place of origin of the muscles, the pelvis was rigidly held by a strong clamp applied to the sacral tuberosity and fixed to the table.

IDENTIFICATION OF NERVES FROM THE FALLOPIAN TUBE AND UTERUS

Nerves were traced to the inferior mesenteric ganglion in the dog from the fallopian tube and the uterus by two entirely different routes. Nerve fibers from the fallopian tubes converged lateral to the ovary, to form a nerve trunk which accompanied the ovarian artery for a distance of 2.5 centimeters, then passed caudally and medially, and subperitoneally, to the inferior mesenteric ganglion. The uterine nerve, made up of fibers which accompanied the branches of the uterine artery from four segments of the uterus, was joined by nerve fibers from the cervix and vagina, and coursed along the uterine artery to a point 2 centimeters caudad to the cervix. From this point it was traced subperitoneally to the inferior mesenteric ganglion. Nerve fibers were teased out under the binocular dissecting-microscope, and afferent fibers were identified under the high power microscope.

Before proceeding to the identification of the uterine afferent nerves, I found it necessary to determine the physiological adequate stimulus and to study the characteristics of the normal visceromotor reflex produced.

DETERMINATION OF ADEQUATE IMPULSE AND OF CHARACTERISTICS OF NORMAL UTERINE VISCEROMOTOR REFLEX

A female non-pregnant dog, was prepared for the recording of the visceromotor reflex. The peritoneal cavity was opened by a small midline incision just above the pubis, and the uterus delivered. The shielded electrode was applied to the left nerve at the level of the cervix; the vagina was opened in the midline, anteriorly, and a suitable cannula was inserted in the cervix. A suture was applied around the cervix (care being used to avoid the inclusion of any other structure, such as the sympathetic ganglion posteriorly), to prevent leakage. The cut edges of the vagina were then sutured around the cannula to arrest bleeding. Care was taken to restore the uterus to its normal position, thus preventing any tension on its nerves or attachments. The lower abdomen was then closed, in three layers, so as to prevent the incidental production of extraneous impulses from the viscera or peritoneum, and as a means of supporting the cannula steadily in place. The recording apparatus was then adjusted so as to balance the normal tonus of the muscles with the levers leveled.

The secondary coil was advanced until stimulation of the left uterine nerve produced a strong visceromotor contraction of the left rectus, and a lesser contraction of the right rectus. The pressure bottle was then gradually elevated until it was found that the sudden application of a pressure of 100 millimeters of mercury sufficed to produce a strong simultaneous contraction of both recti. When the pressure was gradually applied, a similar reflex occurred. As illustrated in Figure 1, dilatation of the uterus produced a visceromotor reflex of precisely the same character as that produced by stimulation of the uterine nerve—preceded by the same latent period and followed by a similar refractory period.

The indirect slight reflex contraction, produced in the right rectus by stimulation of the left uterine nerve had double the latent period of that produced in the left rectus—indicating the presence of intercolating neurones across the cord, and the relatively direct relation of the afferent and efferent neurones of the visceromotor reflex arc on the same side (Fig. 1).

A long series of experiments was performed on dogs and cats in various stages of pregnancy in the postpartem period, and in non-pregnant animals

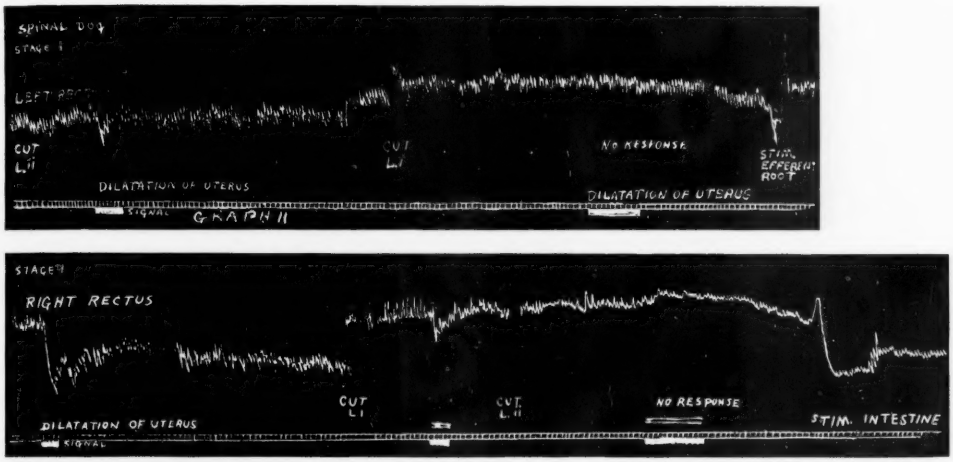


Fig. 2. To illustrate experiments to determine the nerve roots which carry the sensory fibers from the uterus: Series A. i.e. with minimum adequate stimuli (Graph II). Stage I (above) shows the upper limit to be the first lumbar. Stage II (below) shows the lower limit to be the second lumbar.

before the unusual characteristics of the uterine reflex were established. The reflexes occurred consistently even when the muscle was in a state of tremor. A gradual progressive fatigue of reflexes, however, began after a variable period averaging 2 hours (depending upon the condition of the animal and the extent of the operation performed upon it), but the latent period tended to remain the same. Since the visceromotor reflexes disappeared while the animal was still in good condition, an unusually long series would be necessary to determine the uterine afferent nerves. It was found that pregnant animals were unsuitable because the uterine visceromotor reflex was in a refractory state. Although it was found that the refractory state could be removed by intravenous injection of adrenalin, the effect was too transitory to be of practical value in this work. Incidentally adrenalin produced an initial contraction of the rectus fully as strong as that produced by visceral stimulation—indicating a relationship between the sympathetic system and skeletal muscle tonus. It was also found that afferent impulses from the uterus during the first 4 weeks postpartum produced a marked decrease in tone of the abdominal muscles, having the appearance on the graph of an inverted visceromotor contraction.

DETERMINATION OF AFFERENT CONNECTIONS OF UTERUS WITH THE CORD

Series A—with minimum adequate stimuli. A mature non-pregnant female dog was prepared for the recording of the uterine visceromotor reflex by the "sudden pressure" method of stimulation, in the manner described in the first experiment. The animal was then strapped in the prone position; and the spinal cord was exposed by a laminectomy narrow enough to avoid laceration of the vessels, but wide enough to gain access to the posterior dorsal roots, and reaching from the eighth thoracic to the sacrum. Care was taken to avoid touching the cord, and to procure effectual hæmostasis. The dura was then longitudinally incised in the midline. The animal was turned on its right side, and the pelvis was immobilized, and the left rectus was connected to the recording apparatus. The minimal adequate impulse for the uterine visceromotor reflex was determined (100 millimeters of mercury), and the reflex found to be normal. When the upper, cut edge of the dura mater was seized and gently raised up, the fan-like distribution of the sensory fibers from the dorsal nerve roots to the cord was brought into prominence, and could be cut without touching the cord or the efferent root. By this technique, therefore, starting with the cauda equina, in successive order from *below upward*, the sensory roots were divided on the left side. Following each nerve section, a minimal adequate stimulus was applied to the uterus, and the visceromotor reflex recorded.

Section of the sacral roots and lower lumbar roots produced no change in the strength of the response. After section of the second lumbar, the reflex was diminished, though still well marked. When the first lumbar root was divided, the reflex was abolished. That the motor side of the reflex arc was still active was shown by mechanical stimulation of the ventral root (Fig. 2).

The animal was then fixed upon its left side and the right rectus was attached to the recording lever. A minimal adequate stimulus to the uterus was followed by a visceromotor reflex 3 centimeters in depth. The right dorsal nerve roots were then cut

from *above downward* in order to determine the lower limit of the uterine afferent distribution to the cord. After section of the first lumbar, the visceromotor reflex had suddenly diminished to 1 centimeter in depth. When the second lumbar had been divided, there was no response to uterine stimulation. Nevertheless stimulation of the intestine by traction on its mesentery produced a visceromotor contraction (Fig. 2).

Apparently the afferent fibers from the uterus in the dog enter the cord only by the first and second lumbar roots.[1]

Series B—with increasing stimuli showing spread of impulses to adjacent segments through opposite roots. First stage: A mature non-pregnant dog was prepared for experiment in the manner previously described except that the gradual pressure method of stimulation was used in order that pressure could be readily increased. After laminectomy the animal was fixed upon its right side for recording, and the left rectus was attached to the recording apparatus. A strong, sustained visceromotor contraction followed—after a 2 second latent period—dilatation of the uterus with a pressure of 160 millimeters of mercury. In successive order, then, from *below upward* commencing at the fourth lumbar, the left dorsal roots were cut, and an intra-uterine pressure of 160 millimeters was applied after each, while the resulting visceromotor reflex recorded.

After the fourth, third, and second left lumbar were cut, the promptness of response was still the same, and the amount of the visceromotor contraction was undiminished. After the first lumbar was cut, however, there was a sudden prolongation of the latent period from 2 seconds to 5 seconds, and the amount of the visceromotor reflex contraction was suddenly markedly diminished. The depth of contraction measured less than one-third of previous reflexes and the duration of increased tone was also cut down about two-thirds. Section of successive roots and stimulation up to 240 millimeters of mercury produced only slight and further delayed responses; until after the tenth thoracic was cut no response could be elicited. Nevertheless, stimulation of the efferent root produced a strong contraction; and presence of the knee-jerk, and other tendon reflexes showed the animal to be still in good condition. (Graph III, Fig.3).

Second stage: Similar operation in another mature non-pregnant dog, except that the left dorsal roots were cut from *above downward.*

Strong uterine visceromotor reflexes were demonstrated and continued to be characteristic and uniform after the eleventh, twelfth, thirteenth thoracic and first lumbar were cut. Latent period in each case was short and equal. After the second lumbar was cut, latent period was suddenly prolonged by about 3 seconds. The contraction became atypical. It was gradual and shallow, in spite of powerful stimulation (over 240 millimeters of mercury).

After the third lumbar was cut, reflexes from the uterus were still present, but were very shallow and exhibited a similar prolongation in latent period.

Right dorsal roots were then cut, because it seemed apparent that these atypical reflexes were not coming through the left dorsal roots; but must have been relayed across the cord through synapses with the right uterine afferent fibers. As expected, after this possible source of error had been eliminated, uterine dilatation no longer elicited a visceromotor response of any kind.

The cord was then stimulated at its cut end and found to be still very active. That other visceromotor reflexes, having their afferent roots above the cut segments, were still present, was ascertained by pulling on the stomach mesentery, when a strong contraction of the rectus occurred (Graph IV, Fig. 3).

To check these results many similar experiments were performed. Because of the severity and length of necessary operative trauma, and the tendency toward fatigue of reflexes, many experiments were inconclusive. However, a series of ten successful experiments—six of the first stage and four of the second stage, in which the presence of other reflexes at the end showed the animal to be still reacting normally-agreed exactly with the above findings in respect to the localization of the sensory roots of the uterus by the exhibition of normal reflexes. Atypical reflexes with delayed latent period differed, however, in the extent of their spread: depending upon the intensity of stimulus, and the general condition of the animal. These delayed reflexes were demonstrated up to four segments craniad, and two segments caudad to the first and second lumbar, inclusive.

Series C—with increasing stimuli and opposite roots cut. First stage: Similar operation on non-pregnant mature dog except that all right dorsal roots were cut before the experiment was begun on left visceromotor reflexes.

From *below upward* left dorsal roots of the fifth, fourth, third, and second lumbar were cut, and characteristic visceromotor reflexes were elicited. After the first lumbar was divided visceromotor reflexes failed to appear in spite of eight successive well spaced stimulations by intra-uterine pressure beginning at 160 millimeters of mercury and gradually increasing. The motor side of the reflex arc was then shown to be very active (Graph V, Fig. 4). This experiment was repeated in a recently pregnant dog in which the characteristic relaxation, instead of contraction, occurred in response to dilatation of the uterus. These reflexes were abolished after the first lumbar was cut.

Second stage: In a female non-pregnant dog in which all right dorsal roots were cut, before the experiment was begun on the left visceromotor reflexes, the left roots were cut from *above downward.* The visceromotor reflexes were very strong until sud-

[1]The author wishes to thank Professor John Tait of McGill University for his encouragement in the planning and pursuit of these experiments.

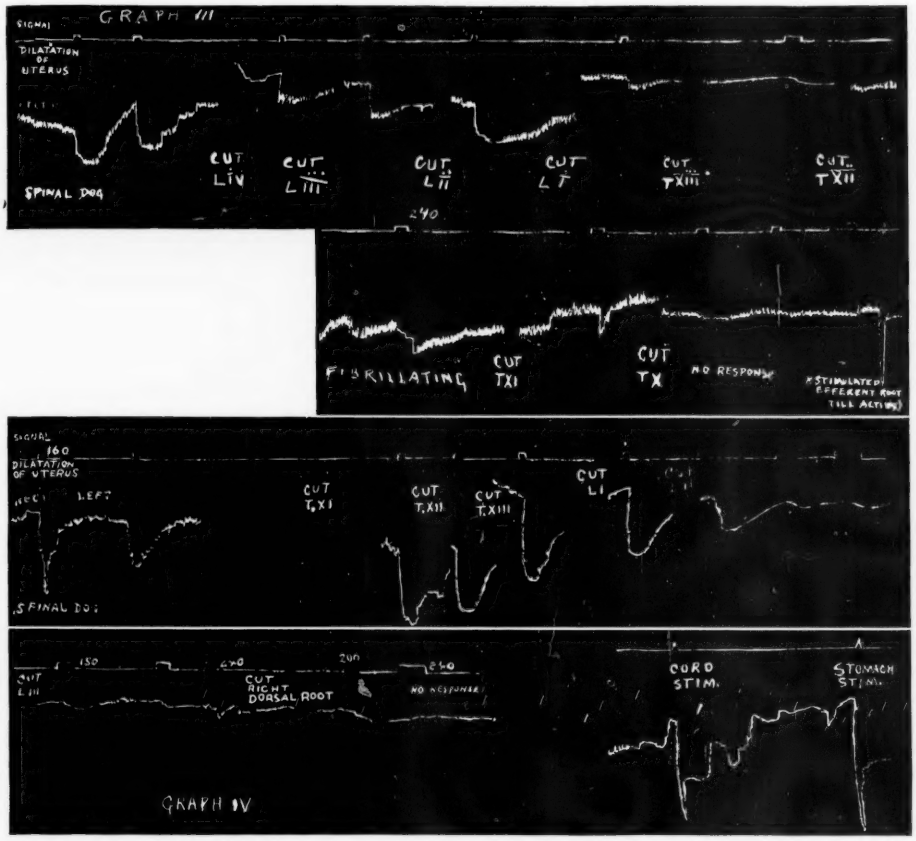


Fig. 3. To illustrate experiments Series B using stimulation strong enough to produce an effect in segments adjacent to the ones receiving the afferent impulses. Stage I (above) shows the upper limit of normal reflexes to be the first lumbar (Graph III). Stage II (below) shows the lower limit of normal reflexes to be the second lumbar (Graph IV).

denly completely abolished after the second lumbar was cut, in spite of very strong stimulation. Then the efferent root was pinched and a strong response occurred (Graph VI, Fig. 4).

DEDUCTIONS AND CORRELATING EXPERIMENTS

1. Afferent fibers from the uterus enter the spinal cord, in the dog, through the first and second lumbar roots.

2. Hyperminimal stimulation (so common in visceral disease) is capable of producing visceromotor effects in segments of the spinal cord adjacent to those which receive the afferent impulses. This spread of afferent impulses along the cord has been demonstrated as far as four segments from the point of entry.

Parturition after section of afferent fibers of uterus. In two dogs, the first and second lumbar nerve roots, and their rami communicantes were resected so as to remove those nerve structures which would ordinarily be anæsthetized by paravertebral block. They became pregnant, and normal parturition occurred at term in each case. It was deduced that the motor mechanism of parturition would not be impaired by a paravertebral block of the afferent roots.

Determination of corresponding roots in man. Although the analogy of the arrangement of afferent nerves in dog and man was well substantiated, the hypothesis that the lumbar

nerve roots were numbered two higher in the dog than in man required experimental proof before the clinical application was undertaken. It was conceived that this could be furnished by the experimental determination in the dog of the segments of the abdominal wall associated with afferent impulses from the fallopian tube, because in man this organ does not usually send sufficiently strong painful impulses to cause spread to segments adjacent to those receiving the afferent impulses, and therefore its afferent supply, by areas of hyperæsthesia, could be relied upon for comparison: eleventh and twelfth thoracic and first lumbar.

In this experiment the visceromotor reflex arc was interrupted on the motor side just lateral to the muscle instead of at the afferent root. By the same method of elimination as before, it was determined that the first, second, and third lumbar nerves only, carried the impulses from the fallopian tube to the rectus. From this experiment the hypothesis was found to be correct, and it was deduced that the uterine afferent roots in the human are the eleventh and twelfth thoracic (Fig. 5).

CLINICAL APPLICATION[1]

CASE 1. Paravertebral block with novocain.

Mrs. F. G. was admitted to the Oregon City Hospital on May 3, 1932, at 9:00 a.m., having pains about every 10 minutes, with a history of six previous labors in each of which she had had prolonged first stage pains (with several remissions) and a rigid os. After several hours in hospital a remission of uterine activity occurred. At 4:30 a.m., May 5, pains recommenced, and by 6 o'clock, were strong, every 6 to 7 minutes. By rectal examination, the cervix was found to be thick and closed and being pushed downward, without dilatation, with each pain. By drawing a pin lightly over the abdomen, in the longitudinal direction, from above downward and from below upward (Head's method), hyperalgesia was found to be confined to an area in the lower abdomen, the upper transverse boundary of which was one-third the distance from the umbilicus to the pubis, and the lower boundary of which was at Poupart's ligament, that is, the eleventh and twelfth thoracic.

With the patient on her left side, at 6:00 a.m., the eleventh and twelfth thoracic nerve roots, on both sides, were injected paravertebrally with 5 cubic centimeters of 1 per cent novocain (Pauchet's method). The patient ceased moaning with her uterine contraction. At 6:20 a.m., the uterus became prominent and on palpation was found to be hard (in strong contraction) but the patient's expression remained unchanged. The uterine contraction lasted 30 seconds. Upon questioning, the patient said that she had felt a "numb sensation, but no pain." The area of hyperalgesia had disappeared and had given place to analgesia over the eleventh and twelfth thoracic segments. During the 3 hours following, twenty-one painless contractions were observed. No change after the sensory fibers were blocked, in the strength of contraction of the uterus could be appreciated by palpation; nor was the frequency or duration of contraction affected. As could be expected from the small amount of novocain required, no toxic effects were observed; and the rate and quality of the heart beats of mother and child showed no change. The patient went into another depression of uterine activity, and since this occurred before the analgesia had worn off there was no return of pain. The cervix had thinned out considerably but was still rigid. The patient was sent home. She later contracted a general impetigo infection, on account of which reinjection was withheld (despite her request for same) when pain recommenced.

CASE 2. Paravertebral block with nupercaine.

Mrs. R. R., weight 260, gave a history of prolonged preliminary pains with her first labor. Due on July 4, 1932, she began to have slight irregular pains at noon on June 26th. By 4 p.m. the pains had become regular every 3½ minutes, lasting about a half a minute but the presenting part was still at the brim of the pelvis.

Hyperæsthesia was found to be confined to the eleventh and twelfth thoracic segments. At 4:45 p.m. the eleventh and twelfth roots were injected paravertebrally, each with 5 cubic centimeters of nupercaine, 1:1,000. During the next hour and a half a record of 29 contractions was made, each lasting from one half to one minute. There was no pain, but the patient was conscious of each contraction, describing it as a numb sensation in the suprapubic region. As far as could be judged by palpation, there was no difference between the painless contractions and those that were observed before the paravertebral block. The areas of hyperalgesia were replaced exactly by analgesia. No significant change in rate or quality of maternal or fetal heart, or any toxic symptoms or signs could be ascertained. At 7 p.m. the patient was still having painless contractions. At 8:30 p.m. analgesia had disappeared. At 8:40 p.m. hyperalgesia was elicited over the eleventh and twelfth thoracic skin segments. By 9:08 p.m. the patient was again complaining of hard pains, seemingly more severe than heretofore. At 9:45 p.m., it was found that hyperæsthesia had extended to include tenth, eleventh, and twelfth thoracic, and third, and fourth lumbar. One hour later pains subsided. Since the patient was in the country, reinjection when labor again started, was not attempted.

CASE 3. Paravertebral and caudal anæsthesia in labor using novocain.

[1]Thanks are due Doctors Guy and Frank Mount, and the nursing staff of the Oregon City Hospital for their co-operation.

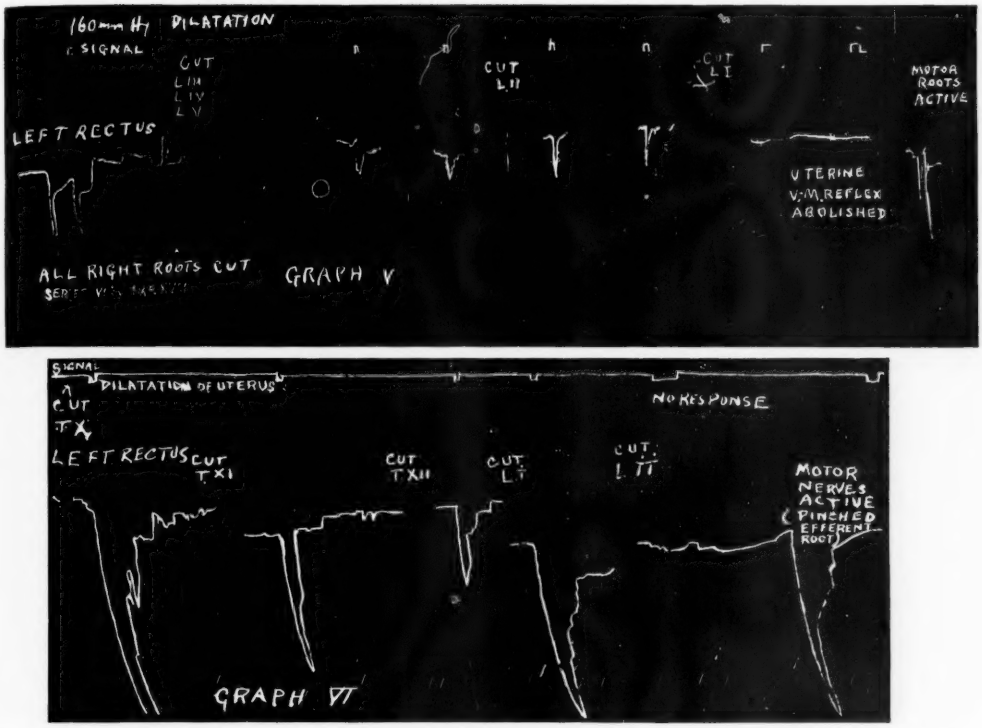


Fig. 4. To illustrate experiments Series C in which, after the opposite nerve roots were cut, no strong stimulus could produce reflexes above the first lumbar or below the second lumbar (Graphs V and VI).

A primipara, Mrs. W. J. V. O., was admitted to the Oregon City Hospital at 5:15 a.m., May 30, having slight pains at irregular intervals. Rectal examination at 6 p.m. showed the cervix to be dilated to a diameter of 5 centimeters. Hyperæsthesia was found definitely to correspond to Head's areas, the eleventh and twelfth thoracic segments, and moderately increased tone was palpated in the lower abdomen corresponding to the area of hyperæsthesia. The patient complained of a steady soreness or backache at the level of the top of the sacrum, chiefly over the left sacro-iliac joint, more severe with each pain. By 6:20, uterine contractions were strong every 3 to 5 minutes lasting for one and a half minutes, causing the patient to cry out loudly for relief. She wanted anything but ether (which had caused vomiting when given for a minor operation, and a prolonged gastric disturbance afterward) and willingly consented to regional block. 6:25 to 6:35 p.m., injection of both eleventh and twelfth thoracic nerve roots paravertebrally with 5 cubic centimeters, novocain 1 per cent. 6:40 to 6:44 p.m., two strong uterine contractions palpated, but complete analgesia, except for pain in back which persisted as a soreness. 6:47 p.m., strong uterine contraction of 35 seconds duration, without crampy pains, and the soreness in back "not as bad as it was." 6:51 to 7:03 p.m., five strong uterine contractions without cramp-like pain, lasting between one, and one and a half minutes. Patient states she feels like going to sleep, as backache is better. 7:05 to 7:15 p.m., six contractions with slight suprapubic cramp-like pain at onset, increasing in severity with each pain.

Hyperæsthesia was found to be now present over the twelfth thoracic area, whereas the eleventh was still analgesic. Apparently the twelfth root had been inadequately blocked. Rectal examination showed labor to be proceeding with cervix now 8 centimeters in diameter. Fetal heart was loud, rate 140. 7:15 to 7:45 p.m., analgesia in eleventh segment remained constant while contractions continued every 3 to 5 minutes with pain. 7:50 p.m., reinjection twelfth thoracic using adrenalin and novocain (mm. 1 to 5 c.cm.). 8:00 to 9:15 p.m. cramp-like pain abolished while strong contractions continued at 2 to 3 minute intervals, but pain (of stretching?) felt low down in the region of the symphysis pubis and in the back. 9:16 p.m., caudal block with 35 cubic centimeters of

novocain 1 per cent, with adrenalin, was followed by cessation of all pain. Uterine contractions then stopped. Analgesia had extended up to the level of the ninth thoracic segment and down the legs.[1] Cervix fully dilated. Patient vomited. Fetal heart strong, 148. 10:35 p.m., palpable strong contractions about one minute in duration, every 5 minutes with only an ache in left sacral region. 11:00 p.m., paravertebral analgesia had worn off and patient is complaining of cramp-like labor pains. Sodium amytal, 6 grains, was given. 12:30 to 1:40 a.m., pains every 2 minutes. Patient crying out for another nerve-blocking injection. 1:40 a.m., caudal block with 20 cubic centimeters novocain 1 per cent abolishing the stretching pains in the region of the symphysis pubis and back, but not affecting pains of contraction. No toxic symptoms appeared in either mother or child. 2:39 a.m., delivery was completed by low forceps, without causing pain; and relaxation was so complete that there was not the slightest abrasion of the perineum. The baby was unusually prompt to stretch its arms and legs, to cry lustily. The placenta was expressed intact at 2:50 a.m. Total blood loss measured 6 ounces. The tone of the uterus remained good. Baby regained birth weight on fifth day. Involution of the uterus was normal.

CASE 4. Paravertebral block, novocain with epinephrine and caudal, nupercaine without epinephrine.

Mrs. J. W. a multipara at term, was admitted to the Oregon City Hospital, at 2:35 p.m., June 28, 1932, with slight irregular labor pains. By 8:30 p.m. she was complaining of strong pains, at 4 to 5 minute intervals, lasting 20 to 30 seconds. Rectal examination showed the cervix to be ½ centimeter thick and 2 centimeters in diameter. Hyperæsthesia was elicited over the eleventh and twelfth thoracic areas. At 9:00 p.m., the eleventh and twelfth roots were injected paravertebrally, each with 5 cubic centimeters of 1 per cent novocain, plus epinephrine, and the pain of uterine contraction was no longer felt. Hyperæsthesia had disappeared and given place to analgesia over the same area. Blood pressure was 140/80. Uterine contractions were so strong that it was presumed that labor would be completed within 4 hours and caudal block was therefore given at 9:40 using 20 cubic centimeters nupercaine 1/500. Patient was now completely comfortable, while at intervals of 2½ to 5 minutes, the uterus went into strong contraction, rising up into a round hard ball. Between 9:45 and 11:30 p.m. 25 such contractions were observed—lasting from ½ to 1¼ minutes, becoming progressively longer and stronger, but without the slightest sensation of pain. At 11:30 p.m. examination showed that labor was progressing, the head being much lower and the cervix thinned out and dilated to 8 centimeters in diameter. The fetal heart was heard loudly in the right flank at 160. From 11:30 p.m. to 12:30 a.m. the patient continued to be free from pain, but had a numb feeling of tightness in the lower abdomen, while contractions proceeded every 3 minutes. At 11:45 p.m., hyperæsthesia was found to be returning to the eleventh and twelfth thoracic areas, but analgesia was still present to deep pinching. Analgesia was still present in the perineum, showing caudal anæsthesia to be still active. At 12:00 p.m. "show" appeared (with dilatation of the cervix), and the patient was instructed to bear down with contractions. At 12:33 a.m., 3½ hours after paravertebral injection, the patient began to have pain with contractions, which were of the same character and frequency as before. At 12:50 a.m., there was some "bulging" and the membranes were ruptured. The presentation was persistent occiput posterior. At 1:30 a.m., under light ether anæsthesia, as the pain had become severe, paravertebral block was attempted, with 5 cubic centimeters of ½ of 1 per cent novocain. On coming out of anæsthetic, patient still complained of pains, and it was found that the perineal analgesia had disappeared. Instead of repeating the caudal block, in this case, ether was given while the baby was delivered by Scanzoni rotation at 2:10 a.m. The baby cried well spontaneously. The placenta was delivered intact at 2:20 a.m. Blood loss was not abnormal. The fundus remained firm. No sedative of any kind was used until after the effect of the regional anæsthetic had worn off. No toxic effects were observed.

CASE 5. Paravertebral block with nupercaine 1:1,000 and epinephrine, and caudal block with nupercaine 1:500 and epinephrine.

Mrs. R. B., age 35, was admitted to the Oregon City Hospital on June 21, 1932, with pre-eclamptic toxæmia of 3 months' duration, becoming severe during the preceding week. She gave a history of chronic invalidism and difficult labors. After a week of medical treatment her blood pressure was 182/114, pulse 118, hæmoglobin 59 per cent, albumen 2 plus, phenolsulphonephthalein total output 23 per cent, and toxic symptoms became severe. On July 1, 9:30 a.m. caudal block with 20 cubic centimeters of nupercaine 1:500 plus epinephrine was given, and a Voorhees bag painlessly inserted. Patient continued to be comfortable, except for an occasional slight contraction-pain, until 3 p.m., when she began to complain of regular pains. At 3:30 p.m. hyperæsthesia was found in the eleventh and twelfth thoracic areas, and analgesia was still present in the perineum from caudal block of 6 hours previous. At 4 p.m. paravertebral injection of eleventh and twelfth thoracic roots on each side (using 5 cubic centimeters of nupercaine 1:1,000 to which had been added epinephrine) was done. The cramp-like pain of uterine contraction was immediately abolished. The bag was expelled at 4:15 p.m. At 4:40 p.m. labor was progressing satisfactorily with painless contractions every 2 to 4 minutes. Cervix was 8 centimeters dilated.

As the analgesia in the perineum disappeared "stretching" pains were felt low down in the region

[1]Such a diffusion along the extradural space to higher nerve roots was prevented in subsequent injections by using only 20 cubic centimeters for caudal anæsthesia. The possibility of variability in anæsthesia of the birth canal could be avoided by blocking the individual afferent roots should the experimental determination of their location be accomplished.

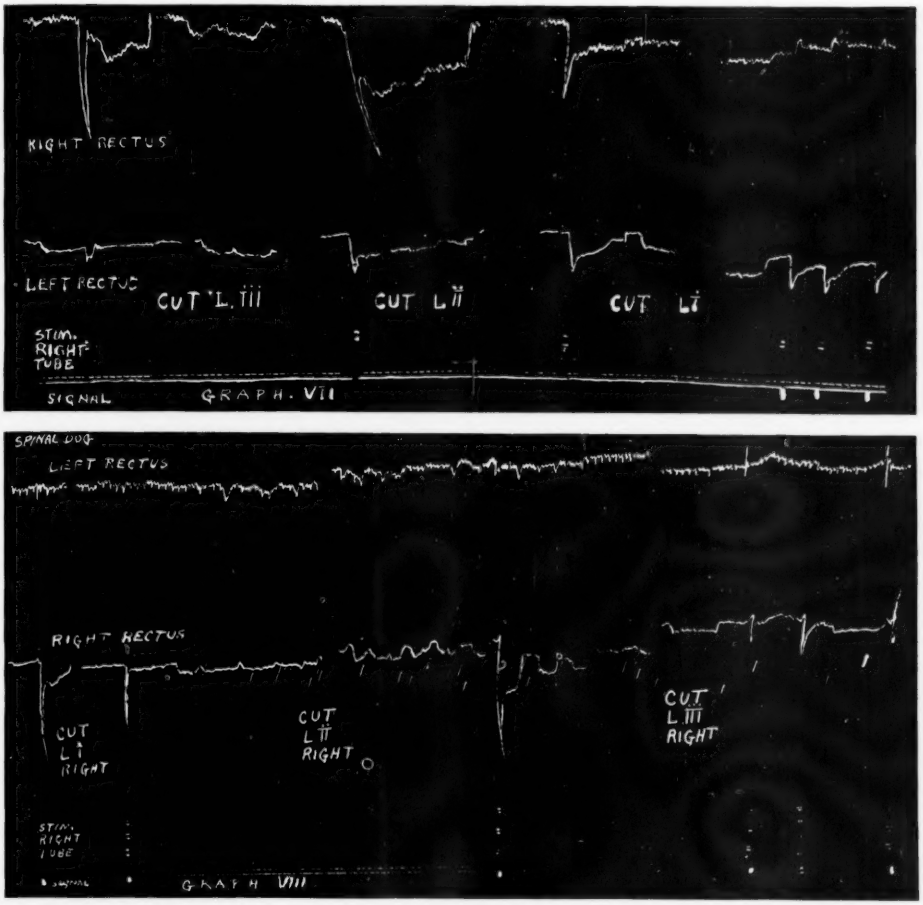


Fig. 5. To illustrate the experiments to determine the segments of the abdominal musculature involved (by hypertonicity) in stimulation of the right fallopian tube, i.e. Graph VII, the upper limit reached after the first lumbar was cut, Graph VIII, the lower limit reached after the third lumbar was cut. The tonus of the left rectus is simultaneously recorded above as a control.

of the symphysis pubis becoming severe enough to require repetition of caudal block at 6:45, 20 cubic centimeters of nupercaine 1:1,000 and novocain 1 per cent, equal parts. After this the only remaining discomfort was a feeling of fullness in the bladder aggravated with each contraction. This was relieved by catheterization of about 16 ounces. Spontaneous delivery occurred at 7:35 p.m. without the mother being aware of the birth. The baby cried promptly and well. The placenta was expressed at 7:48 p.m. One cotyledon was missing and was removed manually without pain. Blood loss was unusually slight. The fundus remained firm. There was no pain of contraction felt at any time during the labor after the paravertebral block. No sedative was given after the preliminary hypodermic preceding bag induction. Mother's pulse, palpated steadily from caudal block to delivery remained steady at 104, and no toxic effects of anæsthetic were apparent at any time during the labor.

CONCLUSIONS

1. The pains of labor are made up of two components, namely: (a) that due to uterine contraction which is transmitted by afferent fibers through the eleventh and twelfth thoracic roots; (b) that due to stretching of the

birth canal, which is transmitted through certain undetermined sacral roots.

2. Paravertebral block of eleventh and twelfth thoracic roots will abolish the pain of uterine contraction for a length of time varying with the type of anæsthetic used, without appreciably affecting the tone of the uterus or the degree, frequency, or duration of contractions.

3. The pain of dilatation of the birth canal may be abolished by caudal block with about 20 cubic centimeters of novocain 1 per cent or nupercaine 1:500 for varying lengths of time dependent on the type of anæsthetic used, without depressing the tone or contractions of the uterus.

4. While the eleventh and twelfth thoracic roots are blocked, there is no hyperæsthesia; whereas in the absence of such anæsthesia the painful impulses may spread in the cord to produce hyperæsthesia in other segments adjacent to those receiving the painful impulses.

5. The combination of paravertebral and caudal anæsthesia, in a safe dosage, is feasible in labor, and the block, which may last as long as 8 hours, may be safely repeated.

BIBLIOGRAPHICAL REFERENCES

1. Bardeen, Charles Russell. A statistical study of the abdominal and border nerves in man. Am. J. Anat., 1901–1902, i, 203.
2. Behan, Richard J. Pain, Its Origin, Conduction, Perception and Diagnostic Significance. New York and London: Appleton & Co., 1920.
3. Cannon, W. B. Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses. Am. J. Physiol., lxxxix, 92.
4. Cleland, J. G. P., and Tait, John. Nervous connections of the mammalian spleen including an account of certain viscero-motor and other abdominal reflexes. Quart. J. Exper. Physiol., Sutherland Simpson Memorial Volume, 1927, 179–204.
5. Cosgrove, S. A. Experience with lumbar anæsthesia in obstetrics. Am. J. Surg., 1932, xvi, 466.
6. Cotte, G. Sur le traitement des dysmenorrhees rebelles par la sympathectomie hypogastrique periarterielle ou la section du nérf présacré. Lyon méd., 1925, lvi, 153.
7. Cunningham. Text-book of Anatomy. 5th ed., p. 1321.
8. Dellepiane, G., and Badino, P. L'Anestesia Paravertebrale in ostetrica e ginecologia. La Clinica ostetrica. October, 1927, xxix, Fasc. 10.
9. Edgeworth, F. H. On a large-fibered sensory supply of the thoracic and abdominal viscera. J. Physiol., 1892, xiii, 260.
10. Fontaine, R., and Herrmann, L. G. Clinical and experimental basis for surgery of the pelvic sympathetic nerves in gynecology. Surg., Gynec. & Obst., 1932, liv, 133.
11. Gertsmann, Max. Discussion on the innervation of the uterus in connection with a case of confinement of a woman paralyzed by a cord lesion. Monatschr. f. Geburts. u. Gynaek., 1926, Vol. lxxiii.
12. Gwathmey, J. T. Anaesthesia. 2d ed., p. 732. New York and London. The Macmillan Co., 1925.
13. Ibid., p. 485.
14. Head, Henry. On disturbances of sensation with especial reference to the pain of visceral disease. Brain, 1893, xvi, 1–132.
15. Idem. Certain aspects of pain. Brit. M. J., 1922, i, 3184.
16. Johnston, J. B. Nervous System of Vertebrates. Philadelphia: P. Blakiston's Son & Co., 1906.
17. Kappis and Gerlach. Paravertebral injection of procaine in diagnosis. Med. Klin., 1923, xix, 1184–1187.
18. Kuntz, Albert. The Autonomic Nervous System. Philadelphia: Lea and Febiger, 1929.
19. Leriche, R., and Stricker, P. Reserches expérimentales sue le nerf présacré. Bull. et mém. Soc. nat. de Chir., 1927, liii, 819.
20. MacKenzie, Sir James. Symptoms and Their Interpretation. New York: Paul B. Hoeber, 1912.
21. Pauchet, Victor. Cited by B. Sherwood-Dunn. Regional Anesthesia. (Victor Pauchet's Technique.) p. 145. London: F. A. Davis Co., 1920.
22. Pottenger, F. M. Symptoms of Visceral Disease. 4th ed. St. Louis: The C. V. Mosby Co., 1930.
23. Ramstrœm, M. En undersokning ofver nervfordelningen i framre bukvaggen i synnerbet i dess peritoneum. Hygiea, 1904, ix, 675–686.
24. Riemann. Cited by Whitehouse and Featherstone. Some observations on innervation of the uterus. J. Obst. & Gynæc. Brit. Emp., 1923, xxx, 565–577.
25. Rein, G. Plexus nerveux fondamental de l'uterus. Soc. de Biol., 1882.
26. Sherrington, C. S. Integrative Action of the Nervous System. p. 91. London: A. Constable & Co., 1906.
27. Shir, M. M., and Darchman, I. The use of sodium amytal in labor. Am. J. Obst. & Gynec., 1932, 115–117.
28. Simpson, Sir James. 1871. Cited by Whitehouse and Featherstone, loc. cit.
29. Swetlow, George T. Am. Heart J., 1926, i, 393.
30. Whitehouse, B., and Featherstone, H. Some observations on innervation of the uterus. J. Obst. & Gynæc. Brit. Emp., 1923, xxx, 565–577.

Thanks are due to the staff of the Oregon Medical School Library for their kind assistance in locating references, and in translations, also to the Surgeon General's Library.

THE CHEMICAL COMPOSITION OF AMNIOTIC FLUID

A Comparative Study of Human Amniotic Fluid and Maternal Blood[1]

A. CANTAROW, M.D., HARRY STUCKERT, M.D., F.A.C.S., and RAYMOND C. DAVIS, M.D., Philadelphia

MAKEPEACE and his co-workers, in a recent communication, make the following statement: "The source and nature of the amniotic fluid, its rate of formation, the mode of reabsorption, if reabsorption occurs, the factors which govern its volume, are all matters of conjecture concerning which but little data exist. Even the chemical composition has been studied in detail by only one modern investigator. This interesting and important fluid is not mentioned in most textbooks of physiology and biochemistry." Various conceptions of its origin attribute it to fetal urine, to transudation from maternal blood, secretion by the amniotic epithelium and to a combination of several factors. Zangemeister and Meissl, and Makepeace, Fremont-Smith, Dailey and Carroll, are of the opinion that although the amniotic fluid may originate as a dialysate in equilibrium with the maternal and fetal body fluids, as pregnancy advances the fluid becomes progressively more diluted by fetal urine. On the basis of available experimental data, this hypothesis would appear to be the most logical. However, in view of the relative paucity of material, no definite statement can be made in this connection at the present time.

The present investigation consists of determinations of the protein, non-protein nitrogen, uric acid, sugar, calcium and phosphorus concentrations of amniotic fluid and maternal blood obtained simultaneously from 36 essentially normal patients. The amniotic fluid was obtained by one of three methods. In a few instances, during the seventh to the ninth months of pregnancy, it was obtained by direct puncture of the amniotic sac through the abdominal and uterine walls, a long needle and a syringe being used. In the great majority of cases at term, the unruptured membranes were punctured by a needle attached to a syringe either when they presented at the vulva or when the uterus was opened at cæsarean section. Cloudy fluids were centrifuged, the chemical determinations being made upon the clear, supernatant fluid. Whole blood, obtained by venupuncture, was used for the estimation of non-protein nitrogen, uric acid and sugar and serum for the estimation of total protein, calcium, and inorganic phosphorus. Total protein was determined by a micro-Kjeldahl method, direct nesslerization being employed (Hawk), calcium by the Clark-Collip modification of the Kramer-Tisdall procedure, inorganic phosphorus by the method of Youngberg, non-protein nitrogen by the method of Folin and Wu, uric acid by the method of Benedict, and sugar by the method of Benedict.

PROTEIN

The protein content of the maternal blood serum varied from 4.07 to 7.5 grams per 100 cubic centimeters, averaging 6.06 grams. Clinically demonstrable œdema was not present in any case and the protein concentration bore no apparent relation to the duration of pregnancy. Makepeace and his associates obtained values, at term, ranging from 5.3 to 6.8 grams, with an average of 6.1 grams per 100 cubic centimeters. The protein content of blood serum during pregnancy thus appears to be slightly lower than that of normal, non-pregnant women, which averages 7 grams per 100 cubic centimeters or slightly higher. These findings coincide with those of most observers. Oard and Peters; Coetzee; and Plass and Bogert found that the serum protein concentration fell to an average of about 6.2 per cent during the first 6 months of pregnancy, gradually rising to reach 6.9 per cent at term. Oberst and Plass later reported an average of 6.9 per cent in early and 6.4 per cent in late pregnancy.

The protein content of the amniotic fluid in this series varied from 0 to 1.5 per cent, averaging 0.53 per cent. This figure corres-

[1]From the Laboratory of Biochemistry and the Department of Obstetrics, Jefferson Hospital, Philadelphia, Pa.

ponds exactly with that reported by Taussig, but is higher than the values obtained by Zangemeister and Meissl and Makepeace, who report average values of 0.22 and 0.23 per cent respectively.

NON-PROTEIN NITROGEN

The non-protein nitrogen content of the maternal blood serum ranged from 13.76 to 36 milligrams per 100 cubic centimeters, averaging 23.98 milligrams. Many investigators, including Caldwell and Lyle; Harding, Allin and Van Wyck; Killian and Sherwin; and Krebs and Briggs, have found that the non-protein nitrogen concentration of the blood falls during the later months of pregnancy, the reduction occurring chiefly in the urea fraction. Harding, in a review of the subject, states that he believes this phenomenon to be due to reduced catabolism of protein during the period when nitrogen is being withdrawn from the mother to supply the increasing demands of the fetus. In a series of 200 other women in the last 3 months of normal pregnancy we have obtained values for blood non-protein nitrogen varying from 17.96 to 36.58 milligrams per 100 cubic centimeters; 8.3 per cent of these ranged from 17.96 to 20 milligrams, 63.6 per cent from 20.01 to 25 milligrams, 26.6 per cent from 25.01 to 35 milligrams and 2.6 per cent were above 35 milligrams per 100 cubic centimeters. In a series of 19 normal pregnant women at term, Makepeace and his co-workers observed values varying between 19 and 32 milligrams averaging 24 milligrams per 100 cubic centimeters.

The latter observers, in a study of the non-protein nitrogen content of the amniotic fluid in 33 cases, found it to range from 18 to 39 milligrams per 100 cubic centimeters, averaging about 27 milligrams. The duration of pregnancy, varying from 2 to 9 months, appeared to have no relation to the non-protein nitrogen content of the amniotic fluid. The amniotic fluid values were higher than those of the blood in 16 instances and lower in 12, there being no definite correlation between the two. In the present series of 36 cases, the amniotic fluid non-protein nitrogen content ranged from 13.6 to 37.5 milligrams per 100 cubic centimeters, averaging 24.25 milligrams, being higher than the blood non-protein nitrogen in 15 and lower in 20 instances. Williams and Bargen, in a series of 11 normal patients, obtained figures of from 16.22 to 35.45 milligrams, averaging 27.05 milligrams, while Zangemeister and Meissl report an average of 23 milligrams as compared with an average maternal blood non-protein nitrogen content of 22 milligrams per 100 cubic centimeters.

URIC ACID

Bunker and Mundell; Harding, Allin and Van Wyck; and Slemons and Bogert have reported observations which appear to indicate that the uric acid content of the blood begins to rise in the late months of pregnancy and continues to increase until the termination of labor. Most observers, however, have failed to substantiate these findings and the general opinion is that the blood uric acid remains within essentially normal limits during pregnancy. Uric acid determinations in 35 cases of the present series yielded values ranging from 1.6 to 4.6 milligrams per 100 cubic centimeters, averaging 3.05 milligrams, the normal limits by the method employed being 2 to 4 milligrams.

Uyeno, in 1919, demonstrated the presence of uric acid in human amniotic fluid but was unable accurately to estimate the amount. Williams and Bargen, in a study of 11 normal cases, report values of 1.93 to 7.73 milligrams, the average being 4.51 milligrams per 100 cubic centimeters. There seemed to be a tendency toward higher values in the later months of pregnancy. In 5 instances simultaneous determinations of uric acid in maternal blood and amniotic fluid revealed consistently higher values in the latter, the average being 5.29 milligrams for the fluid and 3.60 milligrams for the blood. The Folin method was employed by these investigators. In the data presented by Taussig, the uric acid content of the amniotic fluid is given as 10 milligrams per 100 cubic centimeters as contrasted with a fetal blood concentration of 3.2 milligrams per cent. In the present series the uric acid content of the fluid ranged from 2.06 to 8.96 milligrams, averaging 4.54 milligrams per 100 cubic centimeters. There was no apparent

correlation between the maternal blood and amniotic fluid in this respect, the values for the latter exceeding those for the former in 31 instances.

SUGAR

There seems little doubt that pregnancy is associated with some alteration in carbohydrate metabolism as evidenced by the relatively frequent occurrence of glycosuria and decreased glucose tolerance. However, the great majority of observers, including Hellmuth; Shirokauer; and Krebs and Briggs, report normal values for blood sugar during pregnancy. Occasional reports of low and high blood sugar concentrations are encountered in the literature. In our experience there is a distinct tendency toward a low normal or slightly subnormal blood sugar level which becomes more pronounced as the pregnancy progresses. In a group of 200 uncomplicated cases the blood sugar concentration ranged from 46 to 100 milligrams per 100 cubic centimeters (normal limits by the method employed 60 to 100 milligrams); 13.3 per cent were between 46 and 60 milligrams, 65.3 per cent 60.1 to 80 milligrams, 17.3 per cent 80.1 to 90 milligrams and 4.1 per cent 90.1 to 100 milligrams per 100 cubic centimeters. In the present series the figures varied from 48 to 108 milligrams, averaging 84 milligrams in 29 uncomplicated cases, 6 additional patients with mild diabetes mellitus having blood sugars of 109 to 140 milligrams per 100 cubic centimeters.

Williams and Bargen found the sugar content of amniotic fluid to vary from 0 to 35 milligrams per 100 cubic centimeters, averaging 19.6 milligrams in 11 normal cases. Makepeace and his associates observed values ranging from 11 to 86 milligrams, averaging 42 milligrams in the early months of pregnancy and from 11 to 62 milligrams, averaging 33 milligrams, at term. At about the third or fourth month the average sugar content was 58 milligrams per 100 cubic centimeters. Similar observations are reported by Mohs, who found the average value at term to be 26.5 milligrams per 100 cubic centimeters, being higher in the earlier months and decreasing as the weight of the fetus increases. The findings reported by Makepeace were obtained by the Folin method, which yields values from 12 to 20 milligrams higher than those given by the Benedict method which was employed in the present study. In 36 cases the sugar content of the amniotic fluid ranged from 0 to 59 milligrams, averaging 19 milligrams per 100 cubic centimeters. Reference to the accompanying table clearly indicates the absence of any correlation between the sugar content of this fluid and that of the maternal blood. For example, in Cases 34 and 35, with blood sugars of 140 and 135 milligrams, respectively, the amniotic fluid sugar concentrations were 19 and 9 milligrams per cent whereas in Cases 6 and 9, with blood sugars of from 71 to 96 milligrams, the amniotic fluid sugar ranged from 46 to 59 milligrams per 100 cubic centimeters. That glucose constitutes a large proportion of the reducing substance present in the fluid is demonstrated by the work of Makepeace and his co-workers.

CALCIUM

Most observers report a decrease in the level of serum calcium during pregnancy, beginning in the early months and becoming more marked in the later months. Deschamps found that during the first 9 lunar months of gestation the serum calcium remains within normal limits, but that in the last month it is near the inferior limit of normal or slightly subnormal. Widdows noted a low calcium level during pregnancy, with a rise following delivery and in early lactation. Mazzocco observed the average serum calcium in 29 pregnant women to be 8.77 milligrams per 100 cubic centimeters as compared to 9.19 in 19 non-pregnant women. Cantarow, Montgomery and Bolton found that during the course of normal pregnancy and early labor there is a gradual diminution in the serum calcium level from an average value of 10.61 milligrams in the early months to 9.45 milligrams per 100 cubic centimeters at term. Oberst and Plass report the following observations: normal, non-pregnant women, average serum calcium 10.4 milligrams; early pregnancy, 10.4 milligrams; late pregnancy, 9.5 milligrams per 100 cubic centimeters. Other observers, among them Denis and King; and Underhill and Dimick, believe that no change in serum cal-

cium occurs during pregnancy. In the present study the serum calcium concentration in 31 cases varied from 8.2 milligrams to 12.58 milligrams per 100 cubic centimeters, averaging 9.82 milligrams, values which are slightly above those obtained by us in previously observed groups of cases.

Salvesen and Linder, in 1923, noted a parallelism between changes of protein and calcium in sera and transudates from patients with nephritis and heart failure. In some cases of advanced renal failure there was also observed to be a decrease in serum calcium proportional to the increase in inorganic phosphorus which was present in these cases. Later, Peters and Eiserson developed the following mathematical equation to express the relationship between serum calcium, protein and inorganic phosphorus:

$$Ca = 7 - 0.255\ P + 0.556 \text{ protein.}$$

According to these authors, the serum calcium concentration varies directly with that of protein and inversely with that of inorganic phosphorus in the absence of any primary disturbance of calcium phosphate metabolism. Similar observations were made by Cantarow in a study of 14 patients with advanced renal failure. Studies by Greenwald; Stearns and Knowlton; and Oberst and Plass, however, indicate that this mathematical expression cannot be applied in all cases, particularly in conditions other than renal disease. The latter investigators, studying a large group of pregnant women, state that whereas there is a significant correlation between the serum protein and the serum calcium concentrations in non-pregnant and puerperal women, this relationship is completely lost in late pregnancy and parturition, when the protein range is considerably widened. These observations are supported by our data in the present series, which show no such definite correlation between these three factors as was previously seen in patients with renal failure.

There are comparatively few data available regarding the calcium content of amniotic fluid. Merritt and Bauer, in 7 cases, found values ranging from 5.4 to 8.8 milligrams per 100 cubic centimeters, averaging 6.59 milligrams, with serum calcium concentrations of 8.07 to 9.58 milligrams, averaging 8.59 milligrams per 100 cubic centimeters. Makepeace and his associates, in 6 cases, some of which were apparently the same as those reported by Merritt and Bauer, obtained figures for amniotic fluid calcium ranging from 5.3 to 8.8 milligrams averaging 7.1 milligrams per 100 cubic centimeters. In the present study calcium determinations were made on the amniotic fluid in 32 instances; the values obtained ranged from 3.26 milligrams to 7.84 milligrams per 100 cubic centimeters, averaging 5.46 milligrams, being definitely lower than those previously reported. There was no apparent relationship between the calcium concentration in the fluid and its protein and inorganic phosphorus content.

INORGANIC PHOSPHORUS

Normal pregnancy is associated with no significant alteration in the level of serum inorganic phosphorus. Thus, Oberst and Plass report average values of 4.1 milligrams and 3.8 milligrams in the early and late months respectively, as compared with 4.0 milligrams per 100 cubic centimeters in normal, non-pregnant women. In the present series the serum inorganic phosphorus varied from 3.5 milligrams to 5.7 milligrams per 100 cubic centimeters, averaging 4.3 milligrams. The phosphorus content of the amniotic fluid ranged from 1.2 milligrams to 5.4 milligrams per 100 cubic centimeters, averaging 3.1 milligrams. Merritt and Bauer, in 2 cases, obtained values of 0.94 milligrams and 1.2 milligrams per 100 cubic centimeters. As stated previously, neither in the blood serum or in the amniotic fluid was there any demonstrable correlation between the concentrations of calcium, protein, and inorganic phosphorus. Particularly noteworthy is the fact that the phosphorus content of the amniotic fluid was apparently independent of that of the blood serum to a remarkable degree, being actually greater than the latter in 4 instances and practically identical with it in 6 others, the ratio between the two values in the remaining cases being extremely variable.

OBSERVATIONS FROM STUDY

This study was not undertaken with the intention of drawing any deduction regarding

TABLE I.—AMNIOTIC FLUID AND MATERNAL BLOOD SERUM

Case	Month	Protein gm. per cent		NPN mgm. per cent		Uric acid mgm. per cent		Sugar mgm. per cent		Calcium mgm. per cent		Phosphorus mgm. per cent	
		Blood	Fluid	Blood	Fluid	Blood	Fluid	Blood	Fluid	Blood	Fluid	Blood	Fluid
9	7	5.47	0.39	18.4	15.3	1.65	2.06	79	48		5.9	4.5	1.3
12	7	5.31	0.53	13.76	14.85	2.05	2.35	73	37	10.9	5.7	4.6	1.2
16	7	6.12	0.64	21.5	20.1	3.4	4.12	83	31	9.79	4.2	3.9	1.9
19	7	5.09	0.67	28.57	37.5	3.94	4.16	98	11	9.7	3.78	4.0	3.8
2	8	6.2	1.5	25.2	25.8	2.8	2.22	87	21			4.2	2.1
3	8	6.2	0.78	36.0	32.6	2.9	3.7	59	17	9.9	5.54	3.6	1.6
6	8	6.56	0.81	25.2	18.56	2.17	3.65	82	59	8.9	5.7	4.4	1.6
25	8	5.65	0.19	24.28	23.71	3.22	3.36	126	24	11.87	5.0	4.8	5.0
31	8	5.89	0.72	22.38	29.85	2.64	3.52	88	16	12.58	4.16	5.4	4.7
1	9	5.2	0.77	29.5	29.0	2.24	2.54	106	0	8.77	5.52	4.6	2.2
4	9	5.2	0.0	27.8	29.4	2.27	4.76	88	0	9.59	5.21	4.5	3.2
5	9	6.37	0.68										
7	9	6.87	0.48	26.08	30.92	2.68	3.98	96	48				
8	9	7.5	0.48	20.54	13.6	2.71	2.66	71	46			4.4	1.6
10	9	5.05	0.58	19.10	14.92	2.18	2.8	74	22	11.1	7.4	4.9	1.2
11	9	5.1	0.50	21.12	18.75	2.24	2.8	81	23		5.5	5.1	1.6
13	9			20.47	14.01	3.8	6.4	81	23	9.4	5.88	4.2	2.1
14	9				27.27		8.96		19				
15	9	6.8	0.75	29.6	27.7	4.3	7.2	74	7	8.4	3.26	4.2	1.8
17	9	5.26	0.72	21.2	16.5	4.6	6.66	84	34	9.38	4.69	3.5	2.4
18	9	5.93	0.55	27.77	28.57	3.94	5.56	73	22	8.2	5.7	5.5	5.3
20	9	7.06	0.49	26.78	28.3	3.12	4.24	120	13	10.4	4.52	3.6	3.6
21	9	5.15	0.47	27.81	31.74	4.12	5.28	126	13	8.5	5.23	4.6	4.5
22	9	6.64	0.33	28.30	26.08	4.48	5.64	94	25	10.8	5.8	4.9	2.8
23	9	5.79	0.30	23.62	23.71	3.04	3.2	106	26	11.02	6.36	5.3	4.3
24	9	5.36	0.29	30.15	23.24	3.96	4.16	88	22	11.6	7.84	4.5	3.5
26	9	5.27	0.22	24.09	23.81	3.9	3.44	88	9	9.59	5.3	4.9	4.7
27	9	5.34	0.39	26.08	28.16	3.2	5.36	108	18	10.45	7.45	5.7	5.4
28	9	5.77	0.34	32.78	34.28	4.22	7.6	83	18	9.88	3.92	4.5	4.7
29	9	6.79	0.70	24.19	22.30	4.3	5.64	109	16	9.6	5.18	7.0	3.3
30	9	5.68	0.46	21.42	19.34	2.15	2.44	101	26	10.15	6.01	4.8	3.0
32	9	6.56	0.59	20.81	18.74	2.0	2.6	78	17	9.64	7.28	4.9	3.7
33	9	6.51	0.19	21.97	22.54	2.76	2.44	90	8	10.23	6.06	4.2	5.4
34	9	4.07	0.68	26.9	31.74	3.48	6.72	140	19	11.1	4.2	4.2	2.5
35	9			19.86	22.3	1.6	4.86	135	9	11.9	6.07	5.1	2.9
36	9	4.16	0.33	25.63	23.81	2.78	3.16	48	7	11.7	5.88	4.6	4.8
Average		6.06	0.53	23.98	24.25	3.05	4.54	84	19	9.82	5.46	4.3	3.1

the essential nature or mechanism of formation of the amniotic fluid but certain observations may be made on the basis of the data obtained.

One conclusion is apparently justified, namely, that, as believed by Zangemeister and Meissl and by Makepeace and his associates, the amniotic fluid is not, at least at

TABLE II

	Amniotic fluid	Cerebrospinal fluid	Transudates	Maternal blood
Protein*	0–1500	15–40	100–1000	4070–7500†
NPN*	13.6–37.5	12–30	20–40	13.7–36
Uric Acid*	2.0–8.9	0.25–1.0	1–3	1.6–4.6
Sugar*	0–59	40–66	50–90	46–108
Calcium*	3.2–7.8	4.5–5.5	4.5–6	8.2–12.5†
Phosphorus*	1.2–5.4	1–2	1–2	3.5–5.7†

*All values expressed in milligrams per 100 cubic centimeters.
†Determinations made upon blood serum.

term, a simple protein-poor dialysate in equilibrium with maternal or fetal blood plasma. These authors based their conclusions chiefly upon differences in freezing point and chloride content, and consider the amniotic fluid, at term, to be a mixture of fetal urine and what was originally a dialysate of maternal or fetal blood plasma. It is interesting to compare the chemical composition of the amniotic fluid with body fluids believed to represent filtrates or dialysates of the blood plasma, i.e., the cerebrospinal fluid and transudates in the subcutaneous tissue and the pleural and peritoneal spaces.

The protein content of such fluids is usually very low, ranging from 15 to 45 milligrams in the case of normal cerebrospinal fluid and from 0.1 to 1 gram per 100 cubic centimeters in pleural and peritoneal transudates. The values obtained for amniotic fluid are perfectly compatible with the conception of its origin as a dialysate or transudate. It is difficult, on this basis, however, to account for the rather frequent occurrence of higher concentrations of non-protein nitrogen in the amniotic fluid than in the blood. Similar observations are made at times on subcutaneous, pleural and peritoneal transudates, but not nearly so commonly. It may be that analyses of fetal blood and urine will throw some light upon this interesting finding. Perhaps the most important, and certainly the most consistent difference between the amniotic fluid and transudates and dialysates is its relatively high uric acid content, which was found to exceed that of the maternal blood in 31 of the 35 cases examined. It is of interest to note that the uric acid content of six samples of fetal blood ranged from 2.4 milligrams to 7.2 milligrams per 100 cubic centimeters, being higher than that of maternal blood in each instance. This observation may have some bearing on the amniotic fluid uric acid concentration, although contamination by fetal urine may conceivably be a factor of importance. The sugar content of the fluid (0 to 59 milligrams), too, differs greatly from that of cerebrospinal fluid (40 to 66 milligrams) and transudates (50 to 90 milligrams). The calcium content of the amniotic fluid varies within wider limits (3.2 to 7.8 milligrams) and the average concentration (5.46 milligrams) is higher than in the case of other protein-poor body fluids, the calcium content of which apparently corresponds to the diffusible fraction of serum calcium (4.5 to 5.5 milligrams), any increase in protein content being accompanied by an increase in calcium. A similar discrepancy exists in connection with the inorganic phosphorus concentration, which, varying from 1.2 to 5.4 milligrams per 100 cubic centimeters, exceeded that of the maternal serum in 4 cases. The phosphorus content of cerebrospinal fluid and of most transudates ranges from 1 to 2 milligrams, representing from 35 to 50 per cent of the serum inorganic phosphorus concentration. These data, while they throw no light upon the essential nature and mechanism of formation of amniotic fluid, indicate rather definitely that it cannot be regarded as a pure dialysate of maternal nor, perhaps, of fetal blood plasma. The possibility that it represents, in part, contamination by fetal urine, as believed by Makepeace and by Zangemeister and Meissl, cannot be denied on the basis of these observations.

SUMMARY

1. Chemical studies were made of amniotic fluid and maternal blood obtained simultaneously from 36 women in the seventh to the ninth months of normal pregnancy.

2. The protein content of the maternal serum ranged from 4.07 grams to 7.5 grams per 100 cubic centimeters. That of the amniotic fluid varied from 0 to 1.5 grams, averaging 0.53 gram per 100 cubic centimeters.

3. The non-protein nitrogen content of the maternal blood ranged from 13.76 milligrams to 36 milligrams, averaging 23.98 milligrams

per cent, being definitely lower than reported values for normal non-pregnant women. The non-protein nitrogen concentration of the amniotic fluid varied from 13.6 milligrams to 37.5 milligrams averaging 24.25 milligrams, being higher than the corresponding maternal blood values in 15 and lower in 20 instances.

4. The uric acid content of the maternal blood ranged from 1.6 milligrams to 4.6 milligrams, averaging 3.05 milligrams per 100 cubic centimeters. That of the amniotic fluid varied from 2.06 milligrams to 8.96 milligrams, averaging 4.54 milligrams per 100 cubic centimeters and exceeding the maternal blood uric acid concentration in 31 cases.

5. The blood sugar concentration ranged from 48 milligrams to 108 milligrams averaging 84 milligrams per 100 cubic centimeters. (Benedict method, normal range 60 to 100 milligrams per cent.) The sugar content of the amniotic fluid varied from 0 to 59 milligrams, averaging 19 milligrams per cent.

6. The calcium content of the maternal serum ranged from 8.2 milligrams to 12.5 milligrams averaging 9.82 milligrams per 100 cubic centimeters; that of the amniotic fluid varied from 3.26 milligrams to 7.84 milligrams per cent, averaging 5.46 milligrams.

7. The inorganic phosphorus content of the maternal serum ranged from 3.5 milligrams to 5.7 milligrams, averaging 4.3 milligrams per 100 cubic centimeters. The values for amniotic fluid phosphorus varied from 1.2 milligrams to 5.4 milligrams, averaging 3.1 milligrams per cubic centimeter and exceeding the serum phosphorus concentration in 4 instances.

8. These data are compared with corresponding observations on cerebrospinal fluid and transudates. It is believed that the amniotic fluid cannot be regarded as a pure dialysate of maternal blood plasma.

BIBLIOGRAPHY

1. BENEDICT, S. R. The analysis of whole blood. 2. Determination of sugar and saccharoids. J. Biol. Chem., 1931, xcii, 141.
2. BENEDICT, S. R., and BEHRE, J. A. The analysis of whole blood. 3. Determination and distribution of uric acid. J. Biol. Chem., 1931, xcii, 161.
3. BUNKER, C. W. O., and MUNDELL, J. J. The value of blood chemistry in pregnancy. J. Am. M. Ass., 1924, lxxxii, 826.
4. CALDWELL, W. E., and LYLE, W. G. The blood chemistry in normal and abnormal pregnancy. Am. J. Obst. & Gynec., 1921, ii, 17.
5. CANTAROW, A., MONTGOMERY, T. L., and BOLTON, W. W. Calcium diffusibility in pregnancy, parturition and the toxemias of pregnancy. Surg., Gynec. & Obst., 1930, li, 469.
6. Idem. The calcium and inorganic phosphorus content of cerebrospinal fluid and blood serum in chronic glomerulonephritis with uremia. Arch. Int. Med., 1932, xlix, 981.
7. CLARK, E. P., and COLLIP, J. B. A study of the Tisdall method for the determination of blood serum calcium with a suggested modification. J. Biol. Chem., 1925, lxiii, 461.
8. COETZEE, L. J. The plasma proteins in normal and abnormal pregnancy. Proc. Roy. Soc. Med., 1925, xviii, 28.
9. DENIS, W., and KING, E. L. A chemical study of the inorganic constituents of blood in normal and abnormal pregnancy. Am. J. Obst. & Gynec., 1924, vii, 253.
10. DESCHAMPS, A. Le calcium sanguin pendant la grossesse. Bull. Soc. d'obst. et de gynéc., 1927, xvi, 180.
11. FOLIN, O., and WU, H. A system of blood analysis. J. Biol. Chem., 1919, xxxviii, 81.
12. GREENWALD, I. The relation of the concentration of calcium to that of protein and inorganic phosphate in the serum. J. Biol. Chem., 1931, xciii, 551.
13. HARDING, V. J., ALLIN, K. D., and VAN WYCK, H. B. Non-protein nitrogen and uric acid values in blood in pregnancy. J. Obst. & Gynæc. Brit. Emp., 1924, xxxi, 595.
14. HARDING, V. J. Metabolism in pregnancy. Physiol. Rev., 1925, v, 279.
15. HAWK, P. B., and BERGEIM, O. Practical Physiological Chemistry, 10th ed., p. 449. Philadelphia: P. Blakiston's Son & Co., 1931.
16. HELLMUTH, K. Ueber kuenstlich erzeugte Glycosurien und ihre Bewertung fuer die Fruehdiagnose der Graviditaet in der Praxis. Klin. Wchnschr., 1922, i, 1152.
17. KILLIAN, J. A., and SHERWIN, C. P. Some chemical studies in normal and abnormal pregnancies. Am. J. Obst. & Gynec., 1921, ii, 6.
18. KREBS, O. S., and BRIGGS, A. P. Blood studies in normal pregnancy. Am. J. Obst. & Gynec., 1923, v, 67.
19. MAKEPEACE, A. W., FREMONT-SMITH, F., DAILEY, M. E., and CARROLL, M. P. The nature of the amniotic fluid; a comparative study of human amniotic fluid and maternal serum. Surg., Gynec. & Obst., 1931, liii, 635.
20. MAZZOCCO, P., and BUSTOS MORON, R. Le calcium sérique dans les etats gravidiques et puerpéral. Compt. rend. Soc. de Biol., 1921, lxxxv, 692.
21. MERRITT, H. H., and BAUER, W. The equilibrium between cerebrospinal fluid and blood plasma. J. Biol. Chem., 1931, xc, 215.
22. MOHS, H. The normal sugar content of amniotic fluid. Arch. Gynæk., 1931, cxlvii, 532.
23. OARD, H. C., and PETERS, J. P. The concentration of acid and base in the serum in normal pregnancy. J. Biol. Chem., 1929, lxxxi, 9.
24. OBERST, W. F., and PLASS, E. D. The variations in serum calcium, protein and inorganic phosphorus in early and late pregnancy, during parturition and the puerperium, and in non-pregnant women. J. Clin. Invest., 1932, xi, 123.

25. PETERS, J. P., and EISERSON, L. The influence of protein and inorganic phosphorus on serum calcium. J. Biol. Chem., 1929, lxxxiv, 155.
26. PLASS, E. D., and BOGERT, L. J. Plasma protein variations in normal and toxemic pregnancies. Johns Hopkins Hosp. Bull., 1924, xxxv, 361.
27. SALVESEN, H. A., and LINDER, G. C. Observations on the inorganic bases and phosphates in relation to the protein of blood and other body fluids in Bright's disease and in heart failure. J. Biol. Chem., 1923, lviii, 617.
28. SCHIROKAUER, H. Zum Zuckerstoffwechsel in der Schwangerschaft. Berl. klin. Wchnschr., 1912, xlix, 500.
29. SLEMONS, J. M., and BOGERT, L. J. The uric acid content of maternal and fetal blood. J. Biol. Chem., 1917, xxxii, 63.
30. STEARNS, G., and KNOWLTON, G. C. The lack of relationship between the calcium, protein and inorganic phosphorus of the serum of non-nephritic children J. Biol. Chem., 1931, xcii, 639.
31. TAUSSIG, F. J. The amniotic fluid and its quantitative variability. Am. J. Obst. & Gynec., 1927, xiv, 505.
32. UNDERHILL, F. P., and DIMICK, A. The content of inorganic salts in the blood in pregnancy. J. Biol. Chem., 1923, lviii, 133.
33. UYENO, D. The physical properties and chemical composition of human amniotic fluid. J. Biol. Chem., 1919, xxxvii, 77.
34. WIDDOWS, S. T. Calcium content of the blood during pregnancy. Biochem. J., 1923, xvii, 34.
35. WILLIAMS, J. L., and BARGEN, J. A. The uric acid content of human amniotic fluid. Am. J. Obst. & Gynec., 1924, vii, 406.
36. YOUNGBERG, G. E., and YOUNGBERG, M. V. A system of blood phosphorus analysis. J. Lab. & Clin. Med., 1930, xvi, 158.
37. ZANGEMEISTER, W., and MEISSL, T. Vergleichende Untersuchungen ueber muetterliches und kindliches Blut und Fruchtwasser nebst Bemerkungen ueber die totale Harnsekretion. Muenchen. med. Wchnschr., 1903, i, 673.

NON-SPECIFIC GRANULOMA OF THE GASTRO-INTESTINAL TRACT

JOHN F. ERDMANN, M.D., F.A.C.S., NEW YORK
Professor of Surgery, Columbia University, Post Graduate Department; Director of Surgery, New York Post Graduate Hospital

C. V. BURT, A.B., M.D., NEW YORK
Instructor in Surgery, Columbia University, New York Post Graduate Medical School and Hospital

NON-SPECIFIC granulomata are chronic inflammatory, tumor-like masses which may involve any portion of the gastro-intestinal tract. These generally are non-circumscribed infiltrations, extending throughout several inches of the enteric wall. Some of them are fairly well circumscribed and involve only a portion of the circumference. These masses strongly suggest cancer or tuberculosis, and the presence of mesenteric adenopathy further tends to confirm this suspicion.

It is noteworthy that a paper by Braun, in 1909, served to call attention to non-specific inflammatory tumors, and furnished the emphasis to further investigation along this line. Practically all of the literature dates from the publication of his article.

PATHOLOGY

The vast majority of these non-specific tumor-like masses have been reported as occurring in the colon, though in a few instances they have been found in the small intestine, the stomach, the mesentery with secondary involvement of the intestinal wall, and in one instance in the pancreas. These masses vary greatly in size and form, and produce a constriction of the lumen of the gut. The most common type develops predominantly in the wall of the intestine, is not circumscribed, and extends through a considerable length of the enteric wall, while those which begin in the mesenteric area and involve the wall of the intestine by direct continuity are more apt to be circumscribed. Adhesions to the adjacent viscera and parietal peritoneum are frequent.

In one of our cases (Case 1), which is typical of this class of cases, the terminal 2 feet of the ileum, the cæcum, and the first part of the ascending colon were markedly infiltrated, resulting in extensive encroachment upon the lumen. The maximum thickening occurred in the terminal 6 inches of the ileum (Fig. 1), producing an almost complete occlusion of the canal, with marked dilatation of the ileum and constriction of the cæcum. The mucosa of the terminal ileum was extensively ulcerated. Large areas of mucosa were absent in places, suggesting coalescence of smaller ulcerated surfaces. In other places small ulcers were present, with intervening polypoid projections of mucosa (Figs. 1 and 2), which seem to be remnants of mucosa not destroyed in the ulcerating process. In another of our cases (Case 2), the terminal 2 feet of the ileum and the cæcum were involved in the inflammatory process. In this case there was a marked thickening of the ileum and cæcum, with a maximum in the cæcum, producing an almost complete occlusion of the lumen at the ileo-cæcal junction. The mucosa of the ileum and cæcum was extensively ulcerated.

There is a marked œdema and infiltration of all of the coats of the involved portion of the gastro-intestinal tract in those cases in which the tumor develops primarily in the intestinal wall. In our cases all of the layers of the wall were involved, though the greatest amount of thickening occurred in the serosa. Wilensky stated that these tumors involve all of the coats of the intestine, and that the infiltration is most prominent on the mucosal aspect in the majority of instances. The thickening of the serosa results in a distortion of the other layers and a progressive encroachment upon the lumen of the gut until it can no longer permit the passage of its contents.

The mucosa usually presents numerous small, irregular, ragged, superficial ulcerations, accompanied in some instances by innumerable polypoid outgrowths, which would seem to be the result of proliferation of the islands of mucosa not destroyed in the ulcerative process (Figs. 1 and 2). Wilensky stated that in those cases in which the tumor mass involved the wall of the intestine primarily

there was ulceration, which was superficial and not extensive, while in those instances in which there was involvement of the wall by extension from the mesenteric attachment, the mucosa appeared perfectly normal or slightly thickened.

Microscopically these granulomatous masses show, in addition to ulceration of the mucosa (Fig. 2), wide variations in the fibroblastic changes and in the cellular content, varying from a richly cellular, active inflammatory tissue to a firm, dense fibrous cicatrix. Abscesses are seen not infrequently in the indurated and thickened wall, not being confined to any particular layer. The connective tissue stroma is made up of fibroblasts, presenting numerous polymorphonuclear leucocytes, lymphocytes, eosinophiles, plasma cells, and mononuclear cells (Fig. 4). An area containing mast cells and large groups of lymphoid cells can be easily mistaken for carcinoma, while the small round cells may so predominate the picture as to make the tumor resemble sarcoma. The blood vascular changes vary from newly formed channels to those presenting greatly thickened, well formed walls with surrounding peri-vascular infiltration. The lymph channels in some instances show marked dilatation.

Many of these specimens show in all of the layers of the intestine not infrequent multinucleated giant cells, which appear to be of the foreign body variety (Figs. 2, 3, and 5). These cells are large, have irregular outlines, numerous nuclei irregularly placed, and are located in spaces with smooth outlines (Fig. 5). Symmers states in Case 4 that there are "occasional circumscribed tubercle-like formations composed practically exclusively of atypical giant cells with numerous minute tentacle-like processes stretching out from the cytoplasm and enclosing small, variously shaped, colorless, glazed particles, representing, apparently, foreign bodies." We are not prepared to say what is the nature of these foreign substances. It is suggested, however, that possibly they entered through the disintegrated mucosa.

Moschowitz and Wilensky, after a study of the literature dealing with this malady, arrived at the conclusion that undoubtedly many, if not a majority, of the cases of so-called "hyperplastic tuberculosis of the colon" were really simple granuloma. They stated further that the described lesions of hyperplastic tuberculosis, in the majority of cases, were identical with the non-specific granuloma. Microscopically and macroscopically it is extremely difficult in many instances to differentiate between tuberculosis and non-specific granuloma.

A unique finding was manifested in one of our cases, so far as we can determine. In Case 1, in which the terminal ileum, cæcum, and ascending colon were involved, there was present the greatly thickened terminal ileum and ileocæcal valve, together with a false passage extending from the lower end of the ileum into the cæcum near the region of the base of the appendix removed at a former operation (Fig. 1).

ETIOLOGY

Though the etiological factor in these cases is not known, it is our feeling that there is first an interruption in the continuity of the mucosa as a reaction to the presence of an infectious or toxic agent or an indefinite foreign body, resulting in ulceration of the mucosa. With the destruction of the mucosa, active infection follows and extends into the wall of the intestine, setting up a low grade inflammatory process, which manifests itself in the cellular infiltration and connective tissue formation, which constitute these granulomata.

Senn, in this country, first described the non-specific granulomata. He believed that there was a mechanical disturbance in the blood supply, causing a necrosis of the tissue supplied by the involved vessels. A low grade infection ensued, which a reparative process attempted to circumscribe. As a result of this reparative process, granulation tissue was formed in excess of the destructive forces, and a granulomatous tumor resulted.

It is interesting to comment that in many instances preceding the onset of symptoms and signs leading to operations for granulomata there has been an appendectomy performed. The intervals between these two operations have varied from a few months to

a few years. It does not seem likely that there can be any definite connection between an appendectomy preceding by several years the onset of symptoms and signs leading to an operation for a chronic granuloma. This seems particularly true when the granuloma occurs at a considerable distance from the point of the appendectomy.

Several writers have reported the finding of foreign bodies, such as fruit pits, pieces of bone, silk ligatures, instruments, sponges and towels within the granulomata removed at operation. Tietze reported a cæcal granuloma following appendectomy in which was found the silk thread used to ligate the appendix. Schloffer described inflammatory tumors of the abdominal wall, arising after operations for hernia, in which silk sutures were occasionally found imbedded within the tumor. Schreiber reported a case in which many cherry and plum pits were found in a granuloma of the ileocæcal region. Morian and Jaffe each reported a case in which a piece of bone was found in a granuloma involving the colon. Wolfler and Lieblein have called attention to the frequency with which foreign bodies lodge in the cæcum and set up inflammatory reactions. Senn reported a case in which parts of a fruit cake, eaten 9 months previously, were found to be the nucleus of a granuloma.

Not infrequently these granulomata have been found to form at the site of chronic ulcers of the stomach and intestines, usually following a small perforation of an ulcer. In 1898 Graesser called attention to inflammatory processes in the sigmoid, arising from acquired diverticula, though it is thought that these lesions were generally regarded to be hyperplastic tuberculosis of the intestine. Goto, Monsarrat, Birt and Fisher, Tietze, and Rosenheim, Strauss, Moschowitz and Wilensky, and other writers have reported dysentery or colitis as preceding the onset of these granulomata. Tietze reported one case in which an inflammatory tumor developed in the sigmoid following an irrigation with a strong solution of silver nitrate.

Mock reported the formation of a granulomatous mass at the site of a partial intestinal obstruction which had resulted from

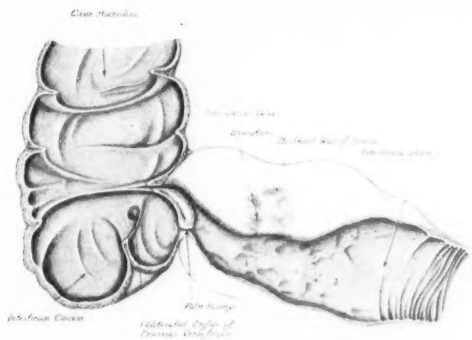


Fig. 1. Drawing of the ileocæcal region of S. G. (Case 1). This presents the characteristic marked thickening of the serosa, containing areas of necrosis and abscess, connecting with the lumen of the ileum. The muscular layer is somewhat thickened and distorted. The mucosa is absent except for polypoid projections, consisting of remnants of the mucosa, with intervening punched out ulcerations. A false passage between the ileum and cæcum is seen near the ileocæcal valve.

pericolic adhesions; another mass at the site of a vesico-intestinal fistula; one around a silk ligature used in the performance of a gastro-enterostomy; another in which the nucleus was a small towel left in the abdomen during a previous cholecystectomy; and still another in the transverse colon secondary to a retroperitoneal lymph gland infection; and one in the pancreas of uncertain origin.

Massive ligatures of the omentum have been reported as causing the formation of these granulomata. Bull, in 1893, Coley, in 1901, and later Braun called attention to the chronic inflammatory thickening of the omentum as a result of its ligature during operations.

SYMPTOMS AND SIGNS

This lesion presents no characteristic clinical concept, though the presence of a mass in the abdomen and stenosis of the lumen of the gut are the most constant findings when the patient seeks surgical aid.

The symptomatology varies with the development of the pathological states. In the early stage, when the lesion is essentially inflammatory, there are no subjective or roentgenologic evidences of obstruction. Mild, aching abdominal pain and local tenderness, with inconstant nausea and vomiting, a py-

Fig. 2. Photomicrograph from Case 1 showing ulceration of the mucosa extending up to the edge of one of the polypoid projections, composed of non-disintegrated mucosa, which has become hypertrophied.

retic reaction of 100 degrees F. and a leucocytosis of 12,000 represent the usual attacks, though occasionally these symptoms become very severe and suggest acute abdominal pathology in the form of acute appendicitis or acute diverticulitis. These complaints are usually of long duration, and have generally shown periods of quiescence and exacerbation.

As the infiltration increases and the pathological state becomes more marked, the symptoms change form, and indicate an obstructive lesion. The attacks become more frequent, the pain more severe and colic-like in type, local tenderness is more marked, nausea and vomiting are more frequent and pronounced, pyrexia and anorexia are more marked, there is increased loss of weight and weakness, and progressive constipation. Not infrequently this infiltration continues until there is almost complete obliteration of the lumen of the gut with its consequent obstipation. In some instances, instead of increasing constipation, there is fluidity of the bowel contents, with frequent evacuations, particularly when the pathology is located in the right half of the colon. When the pathology is present in the left half of the large bowel, constipation is the rule.

One of our patients (M. R.) suffered from very frequent stools for many years preceding the onset of the symptoms and signs leading to the operation for this granulomatous condition.

DIAGNOSIS

This condition is most difficult to diagnose, and prior to operation is generally considered to be a malignant growth, hyperplastic tuberculosis, sarcoma, mesenteric lymphadenitis, appendicitis, or Hodgkin's disease. Syphilitic gumma of the intestine, anthrax and blastomycosis are to be considered.

Even though a definite diagnosis of granuloma cannot be made prior to operation, the chronicity of ill health with exacerbations of good health; increasing constipation; frequent loose stools, with or without mucus or blood; loss of weight; cachexia with or without marked anæmia; anorexia; and the presence of an intra-abdominal mass should cause the surgeon to operate, irrespective of whether or not the roentgenological examination reveals a stenosis of the intestinal tract.

A roentgenological examination is of little value in establishing a definite diagnosis of granuloma. In the early stages of constriction of the lumen, the X-ray findings are most often negative, though with further infiltration of the wall, with its incidental encroachment upon the lumen, evidences of obstruction become noticeable on the roentgenographic plates. The irregular projection of barium into the crevices or extensions from the lumen of the gut into the mass is suggestive of granuloma.

A rapidly developing, marked anæmia is very strongly suggestive of a carcinoma of the cæcum or ascending colon, whereas a fairly normal blood count in the presence of a mass in this region is more indicative of a tumor of the non-specific variety.

TREATMENT

The treatment "par excellence" is operation. Without it most of these patients will progress to a complete obstruction. In the vast majority of instances they are suffering from a partial or complete enteric obstruction before they seek surgical aid or will submit to operative intervention.

The ideal procedure is resection of the involved part of the alimentary tract, after which we prefer to establish an end-to-end or a side-to-side anastomosis and complete the operation in one stage. This is particularly true when the small intestine is the site of the tumor mass. These patients tolerate this procedure very well when it is done with dispatch. In dealing with these tumors of the colon, it may be deemed wise to excise the tumor and establish a double barrelled colostomy preparatory to a secondary closure at a subsequent date. In some instances, where the patient is not a fairly good risk, a preliminary cæcostomy or ileostomy may be performed, followed in 7 to 14 days by extirpation of the tumor mass and re-establishment of the continuity of the intestine. If an abscess is found at the site of one of these tumor masses, simple incision and drainage often will be followed by the disappearance of the tumor and re-establishment of adequate bowel function.

Very often at the time of operation these tumor masses are mistaken for massive cancer, and considered to be inoperable, particularly in the presence of widespread lymphadenopathy. Not infrequently a sidetracking procedure is the requisite to cure the patient. Several cases have been reported in which the tumor mass disappeared following the establishment of a gastro-enterostomy as a palliative measure in the presence of what was thought to be advanced carcinoma of the stomach.

In all cases in which it seems impossible to remove a growth a sidetracking procedure should be done if it is possible. A portion of the mass should be removed for pathological study. Occasionally these masses have been reported as disappearing following simple exploratory laparotomy. However, if the mass does not disappear, the signs of obstruction and inflammatory reaction persist, and the pathologist reports the presence of inflammatory tissue, the surgeon may be justified in re-operating to make a more desperate attempt at removal of the tumor mass or the establishment of a sidetracking route.

The following case reports are presented as representing the pathological entity of non-specific granulomata of the intestine:

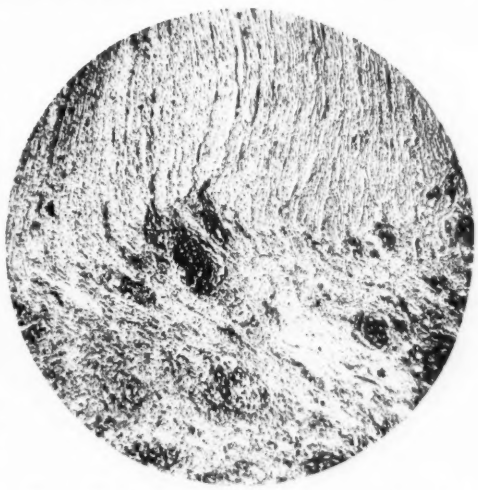


Fig. 3. Photomicrograph from Case 1 presenting œdema and cellular infiltration of the muscular layers. A small abscess is present at the junction of the circular and longitudinal muscle bundles, which show chronic inflammatory reaction, containing foreign body giant cells.

CASE 1. S. G., male, aged 18, No. 64,153, admitted to hospital on April 12, 1931, and discharged on May 12, 1931. His chief complaint was intermittent cramps in the abdomen, bleeding from the rectum, weakness and general malaise for 2 years, and loss of 30 pounds in three years. The family history was negative. Appendectomy was performed without drainage 6 years ago, after which his convalescence was slow. There has been no known tuberculosis contact, and he has had no venereal diseases.

In the past 3 years this patient has lost 30 pounds, and during the last 2 years he has suffered from anorexia, considerable belching and bloating after meals, general malaise, increasing in the past 6 months and frequent colds. He has experienced mild, generalized abdominal cramps two or three times a week during the past 2 years. Six months ago the cramps grew more severe, and became localized to the right lower quadrant. Frequently these cramps have appeared 1 or 2 hours after the ingestion of green vegetables, raw fruit or other roughage, and have lasted for a few minutes at a time. A constant pain has been superimposed on the cramps in the right lower quadrant in the past 4 months and has been severe enough to awaken the patient at night and to interfere with his walking, but not of such intensity as to require morphine. He has applied hot water bottles to his abdomen with some relief. No nausea or vomiting has been present at any time. Two years ago this patient began to feel pain at stool at irregular intervals, and he has noticed a red tinge to the water in the bowl from time to time, and has observed some blood on the toilet

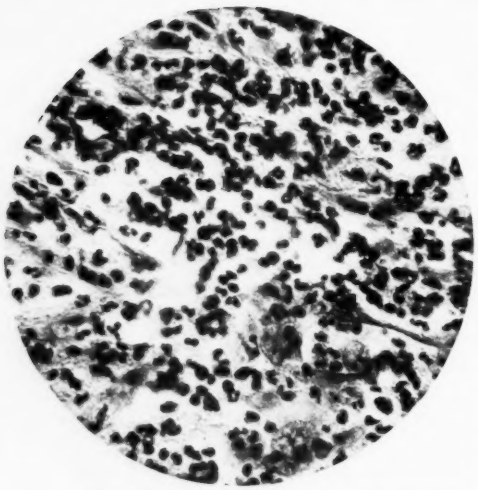


Fig. 4. Photomicrograph of a higher power of the serosa from Case 1, presenting a connective tissue stroma made up of fibroblasts showing numerous polymorphonuclear leucocytes, lymphocytes, eosinophiles, plasma cells, and mononuclear cells, which are the characteristic types of cells found in the inflammatory portion of this tissue.

paper. In the past few months his bowels have moved once a day under the influence of mineral oil once or twice a week. Physical examination revealed a poorly nourished and developed young male appearing very pallid, chronically ill and to have lost considerable weight. His heart and lungs were surgically competent, and his blood pressure was 118/80. His abdomen was soft and not distended. There was present a right lower quadrant scar, just above which was an irregular, somewhat firm, moderately tender, slightly movable mass the size of a lemon.

On admission the blood count showed: red blood cells, 4,340,000; hæmoglobin, 80 per cent; white blood cells, 11,800; polynuclear cells, 80 per cent; blood grouping Jansky I; urinalysis essentially negative. X-ray picture of chest, while in the hospital, was negative for tuberculosis.

Pre-operative preparation: Fluids were forced orally, and retention enemas of 3 ounces each of saline and tap water were given every 4 hours. Colonic irrigations were given night and morning for the 2 days preceding the operation. Pulvis glycyrrhizæ compound drams iii were given the night before the operation, and a colonic irrigation was administered 2 hours preceding the operation. We follow this general routine in all obstructive conditions involving the lower end of the ileum and the colon or rectum.

Operation was performed 2 days after admission, under ether anæsthesia, 3 feet of the ileum, the cæcum, ascending colon, and one half of the transverse colon being resected, and an end-to-end anastomosis was established.

The condition of the patient immediately after the operation was good. Pain was controlled by two or three doses of ⅛ grain morphine in 24 hours for the first 2 days. An occasional dose of ½ grain of codeine sulphate and 10 grains of pyramidon was given for 2 more days. Fluids were tolerated well by mouth after 5 hours. One hypodermoclysis of 1,500 cubic centimeters of 5 per cent glucose in normal saline was given immediately after the operation. Retention enemas of 3 ounces each of saline and tap water every 4 hours were continued into the fourth day. Eleven hours after the operation the patient voided, and his output was satisfactory. Tea and oatmeal gruel were begun on the second day; orange and grape juices were added on the third day, cocoa and milk on the fifth and eggs on the ninth day. This patient subsisted entirely on this diet. *Vomiting* occurred once on the second day. Flatus was expelled through a rectal tube on the first day, and on the second day he passed through the rectal tube on two occasions 10 ounces of dark red fluid resembling blood. On the third day an alum enema was productive of dark yellow fluid and flatus. From the fourth through the nineteenth day there were 3 to 5 yellow fluid stools in 24 hours. Subsequently until discharge there were 2 per day. Temperature, pulse, and respiratory rates showed only slight variations from the normal. Sutures were removed on the eleventh day, and a slight amount of seropurulent discharge was expressed from the wound. A green purulent discharge persisted until the patient left the hospital, at which time the wound was almost healed.

The report by the pathologists of the New York Post Graduate Medical School and Hospital is as follows: Grossly the specimens consist of a portion of the ileum, the cæcum, a portion of the ascending colon and what appears to be a part of the omentum. The appendix is absent. From the gross appearance it is impossible to differentiate between the large and the small intestine. A tumor mass occupies a section of the intestine 10 centimeters in length at the junction of the ileum and the cæcum. Near the tumor mass there are rounded projections which extend into the lumen. The small end of the intestine opens into this tumor mass by a somewhat tortuous pathway, and at one side there is a false passage extending into the lumen of the intestine through the tumor mass near the ileocæcal valve. There are some firm nodules, evidently lymph nodes in the fat outside of the intestine.

Microscopic sections through the tumor mass near the central portion of the specimen, involving principally the ileocæcal region, show the substance to consist largely of inflammatory fibrous and granulation tissue richly infiltrated throughout by abundant lymphocytes, plasma cells, and in some places by very abundant polynuclear leucocytes. There are also rather numerous multinucleated giant cells which appear to be foreign body giant cells. There

are present abundant newly formed blood vessels in some parts of the granulation tissue, and many of the lymph channels are distended to a diameter of ¼ millimeter. Some of the arteries show definite thickening of the walls. Tubercles are not recognized, and there is nothing to suggest the presence of syphilis. Sections from the region of the false passage show highly purulent granulation tissue lining this channel. Sections of the lymph nodes reveal only a chronic inflammatory reaction. Diagnosis: Severe chronic productive purulent inflammation at the junction of the small and large intestine.

Dr. Douglas Symmers, director of laboratories, City of New York, reports on this specimen as follows: "Microscopic examination shows a marked chronic productive inflammatory lesion of the intestinal wall characterized by the overgrowth of connective tissue which in places is rich in small, thin walled, apparently newly formed blood vessels. Scattered through the connective tissue and interpolated between the muscle bundles of the gut are large numbers of richly cellular lymphoid foci of variable shapes and sizes and an occasional one showing an attempt at the formation of germinal follicles. Scattered through these lymphoid collections in places are giant cells of the Langerhans type, most of them associated with the presence of foreign particles, many of which present a smooth, glazed appearance, as if representing, perhaps, some altered form of waxy substance. In still other places are large collections of polynuclear leucocytes, representing abscesses. The lesion histologically appears to be a chronic productive inflammatory process associated with the presence of foreign body giant cells."

Fig. 5. Photomicrograph of submucosa from Case 1, presenting a multinucleated giant cell of the foreign body type in a smoothly outlined space, which was apparently filled with foreign body material. The surrounding inflammatory reaction consists of fibroblasts and the numerous types of wandering cells.

Case 2. I. M., female, aged 39 years, No. 61,679, admitted to hospital January 4, and discharged on February 2, 1932. Her chief complaint was pain in the right lower quadrant of the abdomen, much eructation, and heart burn for the past year, and the loss of 35 pounds in the past 4 months. Pelvic repair with appendectomy and right salpingo-oophorectomy was done 7 years ago and was followed by pneumonia and phlebitis.

About one year ago this patient had two attacks of abdominal pain in the right lower quadrant, both very severe and each lasting 2½ weeks. She experienced nausea and vomiting during the attacks. During the past year she has had digestive disturbances, characterized by great quantities of gas orally, inability to take fried or fatty foods, and by the presence of frequent heart burn. For the past 6 months she has had almost constant pain in the right side of the lower abdomen, which has become more intense at 6 o'clock in the evening. Aspirin and frequently morphine have been required to produce rest. This patient has experienced frequent nausea and vomiting during these 6 months. She has been on a Sippy diet for 6 weeks, and has had no vomiting during this time. There has been no relationship between the appearance of the pain and meals. There has been no blood in the evacuations, though she has been chronically constipated. She has lost 35 pounds in the past 4 months, her best weight being 195 pounds 4 months ago.

Physical examination revealed a young female, appearing chronically ill, and to have lost considerable weight. The heart and lungs were surgically competent, and the blood pressure was 120/80. The abdomen was slightly distended, and there was a low, midline scar from a previous operation. There was slight tenderness in the right upper quadrant and marked tenderness in the right lower quadrant. There was a very tender, rather firm, indefinitely outlined mass occupying most of the right lower quadrant. Slight œdema was present in the right leg.

On admission the bleeding time was 2 minutes, and the coagulation was complete in 4¼ minutes. The urinalysis was essentially negative. Eleven days after the operation the blood count showed: red blood cells 3,280,000; hæmoglobin, 61 per cent; white blood cells, 8,400; and polynuclear cells, 78 per cent.

Operation was performed under ether anæsthesia on the day following admission, with resection of 2½ feet of the ileum and the cæcum. An end-to-side anastomosis was established. Grossly this specimen resembled carcinoma. Two quarts of normal saline were left in the abdomen at the close of the operation. The condition of the patient was good following the operation, though she was very apprehensive and restless for many days. Pain was relieved for the first 2 days with morphine, though subse-

quently rest was provided with luminal, 1 grain, three times a day. An irritating cough developed on the sixth day and persisted for 12 days. A hypodermoclysis was given immediately after the operation, and an infusion the next day. After the second day she retained oral fluids well, though retention enemas were continued through the second day. Slight vomiting occurred on the first day. Flatus was expelled freely after a milk and molasses enema was given on the first day because of considerable distention. On the third day the bowels began to move one to three times a day without enemas or cathartics. These were watery and were so when the patient was discharged from the hospital. The immediate postoperative reaction was mild, although considerable temperature reaction resulted from an extensive fascial slough which became evident after the sixth day.

The report by the pathologists of the New York Post Graduate Medical School and Hospital is as follows: The gross specimen consists of a portion of the ileum and the cæcum. Thirty-five centimeters from the ileocæcal junction there is an ulcerating area 30 by 10 millimeters in diameter in the ileum. Its floor is gray and irregular. On the cæcal side of the ileocæcal junction the wall is thickened to 30 millimeters. This thickening apparently occludes the cæcal pocket. On section the wall is fibrous, and the mucous membrane is highly œdematous. No glands are palpated in the attached fat. There is no appendix. Microscopic sections through the ulcer in the small intestine show abundant fibrinopurulent exudate on the surface of the ulcer. The submucous layer is thickened by increase in fibrous tissue, in which there are moderately numerous lymphocytes and polynuclear leucocytes. The circular muscle coat is hypertrophied. Sections through the wall of the cæcum also show ulceration, which is also covered by abundant fibrinopurulent exudate. The wall of the intestine is greatly distorted by scar tissue in this region, and there is a marked increase of fibrous tissue in the subserous coat. The entire thickness of the wall is infiltrated by wandering cells. There is no evidence of tuberculosis or of neoplasm. Diagnosis: chronic ulcerative inflammation of the lower end of the ileum and of the cæcum.

Case 3. M. R., female, aged 42 years, No. 64,981, admitted to hospital May 11, 1931, and discharged on May 25, 1931. Her chief complaints were pain in the abdomen, which had been intermittent for 11 years, and became worse in the past 2 months; diarrhœa for 11 years; loss of weight; pain in the left kidney region for 4 months. The family history was irrelevant. She had had a nervous breakdown 12 years ago with persistent nervousness; *appendectomy* with drainage 9 years ago, after which she never felt perfectly well; laparotomy 3 years ago for polyps of the uterus; gastro-intestinal X-rays taken in another hospital 7 weeks prior to admission showed only an irritable colon.

Eleven years ago there developed a frequency of bowel movements with as many as 20 in 24 hours, associated with an inconstant burning sensation in the rectum. The movements gradually decreased to three to five a day, and for the 2 weeks prior to admission there were two or three small, watery movements per day. For the past 2 months there has been present a severe aching pain over the right lower quadrant, with marked tenderness. Though in its incipiency principally nocturnal, this pain has been present both day and night, and has been extremely severe during the past 2 weeks. Frequent doses of morphine have been required for its relief in the past 2 months. This patient has experienced pain, insidious in onset, beginning just lateral to the umbilicus and radiating to the left kidney region. These pains have become gradually more severe and have been worse in a reclining position. Her appetite has been poor for 11 years, and anorexia has been marked for several months. Two months ago she vomited some bile streaked with blood, and during the past 6 weeks has vomited almost everything she has ingested. She has lost a great deal of weight in the past 6 months. Physical examination revealed a poorly nourished and developed, pallid, middle aged female, appearing chronically ill. The skin was dry and showed a loss of much subcutaneous tissue. The heart and lungs were surgically competent, and the blood pressure was 108/76. The abdomen was protuberant, more so on the right side. It presented two lower abdominal scars, resulting from previous operations. There was present in the right lower quadrant a very firm, freely movable, very tender, irregular, nodular mass, which extended up to the level of the umbilicus and medially almost to the midline. Over this mass there was flatness, though there was no evidence of fluid in the abdomen.

On admission the blood count showed: red blood cells 3,350,000; hæmoglobin, 61 per cent; white blood cells, 6,400; polynuclear cells, 76 per cent. The blood chemistry and urinalysis were normal.

Operation was performed 2 days after admission. Three feet of the lower ileum were resected, with the establishment of a side-to-side anastomosis. Three pints of normal saline were left in the abdomen at the close of the operation. An infusion of 1,000 cubic centimeters of 10 per cent dextrose in saline was given immediately after the operation. One hypodermoclysis was given the next day, and retention enemas were continued for the first 24 hours. Fluids were tolerated well orally 11 hours after the operation. The urinary output was satisfactory. A soft diet was allowed on the third day, and a regular diet on the seventh day. On the second day, flatus and brown fluid were expelled through a rectal tube, and on the fourth day there was a fluid evacuation, after which patient had one or two movements in 24 hours. Temperature, pulse, and respiratory rates presented nothing unusual. Sutures were removed on the tenth day, when patient was permitted out of bed. She was discharged on the fifteenth day eating a full diet, evacuating formed stools, with her wound healed by primary intention. X-rays of the

chest taken after discharge from the hospital were negative for tuberculosis.

The report by the pathologists at the New York Post Graduate Medical School and Hospital is as follows: Grossly the specimens consist of a portion of the small intestine, a piece of omentum, and of what appears to be a greatly hypertrophied lymph node. The portion of intestine is greatly kinked on itself and held by firm fibrous adhesions. The wall is greatly thickened, measuring 8 to 10 millimeters. On the mucosal surface there are numerous areas of ulceration as long as 100 millimeters, separated by small portion of normal mucosa. In the ulcerated areas there are small bits of mucosa, forming elevated, pedunculated projections. A small amount of purulent exudation is present on the inner surface. The mesentery is also somewhat thickened and fibrosed in places, and contains a few hypertrophied lymph nodes. *Microscopic* sections taken from different regions of the small intestine reveal a greatly thickened, fibrosed, and somewhat œdematous wall. The entire thickness of the wall is infiltrated by a large number of polynuclear, mononuclear and plasma cells. The mucosa is desquamated over large areas, with intervening intact mucosa, and there is a large amount of purulent exudation on its inner surface. At one place immediately below the mucous membrane there is a round area made up of epithelioid cells containing a few giant cells showing central areas of necrosis and lymphocytic infiltration around its periphery. This is a typical tubercle, but there are no other such tubercles found in any sections, although in one place there are seen two multinucleated giant cells of the Langerhans type. Sections of the lymph node show marked hypertrophy, moderate endothelial proliferation, and in places a large amount of necrotic tissue containing numerous polynuclear cells.

Dr. Douglas Symmers, director of laboratories, City of New York, reported on these microscopic sections as follows: "Microscopic examination shows the presence of a chronic productive inflammatory lesion of the gut wall associated with considerable overgrowth of connective tissue and the formation of lymphomatous collections. The mucosa in places is richly infiltrated by circumscribed collections of polynuclear leucocytes, the whole representing abscess formations. In other places the mucosa supports an occasional circumscribed tubercle-like formation composed practically exclusively of atypical giant cells with numerous minute tentacle-like processes stretching out from the cytoplasm and enclosing small, variously shaped, colorless, glazed particles, representing, apparently, foreign bodies."

Case 4. S. B., 60 years, female, in July, 1926, began to complain of belching and bloating after meals and the onset of epigastric pain several hours after eating. She suffered from increasing constipation and general gastro-intestinal disturbances. On August 11, 1926, the roentgenologist at the Nyack Hospital reported as follows: "The gall bladder takes the dye normally. A uniform shadow was present except for a small, irregular shadow near the cystic duct. The stomach appears normal in size, shape, position and in peristaltic action. There is a persistent defect of the duodenal bulb, which is believed to be due to gall-bladder pathology." Following this the patient improved somewhat on diet, medication and mild laxatives. In December, 1926, attacks of apparent gall-stone colic became more frequent and severe. Wassermann reactions taken on two occasions were negative. This patient was admitted to the Nyack Hospital on January 8, 1927, and on the following day was operated on by the senior author.

The gall bladder was pathological, and there was present a large, firm, ulcerative mass involving the terminal ileum, cæcum, and ascending colon, which apparently produced complete obstruction. The gall bladder was removed. The terminal ileum, cæcum, ascending colon, and a portion of the transverse colon were resected, followed by an anastomosis of the ileum to the transverse colon. Drainage was instituted.

After a stormy course this patient was discharged from the hospital with a fæcal fistula, and continued to improve until August, 1927, when evidence of complete intestinal obstruction occurred. On August 28, 1927, her abdomen was reopened, and the fistula was found between the ileum and the colon. A large inflammatory mass was found to have formed in the ileum at the site of the anastomosis, producing a complete obstruction. A section of the ileum, 24 inches in length, was removed, and an anastomosis again established between the ileum and the colon. This patient expired on the sixth day after operation.

Grossly the specimen is a portion of the small intestine 145 by 33 by 52 millimeters. For a distance of 60 millimeters the wall is very markedly thickened, reaching 9 millimeters in places, and there is a sudden change in the mobility of the rugæ of the mucous membrane in this area. There are several small papillary projections of the mucous membrane into the lumen. There is a small fistulous opening leading from the interior into the surrounding fat tissue, into which a probe can be introduced for a distance of 20 millimeters, just at the border of the normal and the thickened mucous membrane. Microscopic sections at the junction of the normal and the markedly thickened wall of the intestine show a sudden increase in connective tissue elements, marked thickening of all of the layers and proliferation of fibroblasts. There are numerous collections of small round cells and several formations of follicles. Some of these follicles simulate tubercles, but in their composition they are not characteristic of nodules produced by the bacillus tuberculosis or its toxin.

Diagnosis: Marked chronic progressive inflammatory process of the small intestine of unknown etiology.

Case 5. E. D., female, 37 years. Her chief complaint was that she had been sleepy most of the time for several months and had generalized abdominal

discomfort for one month prior to admission to the hospital. She had been an invalid for 17 years, suffering from chronic arthritis. Her legs were ankylosed at the knees and hips.

In the latter part of the winter of 1922 this patient felt indisposed, but had no specific complaints except that she felt sleepy most of the time. In September, 1923, she experienced some generalized abdominal discomfort, which was not acute. She was seen by her family physician, who discovered a mass in the right inguinal region.

On October 1, 1923, a large inguinal abscess was incised and drained by the senior author at the Nyack Hospital. Three days later a fæcal fistula developed at the site of the incision. After 10 weeks in the hospital this patient returned home, where her general health continued to improve, though the fistula remained unchanged. On September 16, 1924, this patient was again operated upon by the senior author, who found the right side of the pelvis filled with a large, firm, irregular mass, consisting of the cæcum, part of the ascending colon, and a considerable length of the small intestine. Several feet of the ileum, the cæcum and the ascending colon were resected, followed by an anastomosis of the ileum with the transverse colon. Drainage was instituted. This patient made a satisfactory recovery, and she was discharged on October 23, 1924. On March 22, 1932, she had no gastric or intestinal disturbance, and was in good general health.

At the time of operation the specimen, consisting of numerous coils of intestine firmly matted together, grossly appeared to be identical with these non-specific granulomata. It is regretted that the pathological report has been lost.

PROGNOSIS

The prognosis following operative intervention is excellent. Moynihan, Robson, and others have stated that these granulomatous masses usually disappear following the simple operative procedures in which the visceral contents are sidetracked. This is a most important diagnostic and prognostic characteristic.

CONCLUSIONS

1. Non-specific granulomata are chronic inflammatory tumor-like masses which may involve any part of the gastro-intestinal tract. There is encroachment upon the lumen of the intestine as a result of infiltration, which may predominate in the wall proper or extend from the mesenteric area, and produce an intestinal obstruction.

2. The etiological factor in the production of these granulomata is not known. Foreign bodies have been found in many of the cases reported. It is our belief that ulceration of the mucosa follows a reaction to infection or a foreign body, and that a chronic inflammatory response results in the tumor-like formation.

3. A diagnosis of the non-specific granulomata is usually possible only by microscopic examination of tissue removed at operation. Grossly, these masses are generally mistaken for carcinoma or tuberculosis of the enteric canal.

4. Excision of the tumor mass should be done wherever possible. If removal is not feasible, and obstruction of the bowel is established or imminent, a simple sidetracking anastomosis should be performed. The tumor mass has been said to disappear following a simple laparotomy without any anastomosis of the intestines. A portion of the tumor mass should be removed for microscopic study.

5. The prognosis is excellent following extirpation of the tumor mass or the establishment of a sidetracking route.

6. Clinically, the symptomatology varies with the development of the pathological states. When the lesion is principally inflammatory, there is no evidence of obstruction, though as the infiltration increases with its encroachment upon the lumen of the intestine, there appear signs of intestinal obstruction.

BIBLIOGRAPHY

1. Birt and Fischer. Beitr. z. klin. Chir., 1917, civ, 167.
2. Braun. Arch. f. klin. Chir., 1901, xii, 378; Deutsche Ztschr. f. Chir., 1909, x, 1.
3. Goto. Arch. f. klin. Chir., 1912, xcvii, 190.
4. Jaffe. Verhandl. d. deutsch. Gesellsch. f. Chir., 1908, xxxvii, 218.
5. Mock. Surg., Gynec. & Obst., 1931, lii, 672, 689.
6. Monsarrat. Brit. M. J., 1907, ii, 65.
7. Morian. Deutsche Ztschr. f. Chir., 1912, cxiv, 267.
8. Moschowitz and Wilensky. Am. J. Med. Sc., 1924, clvi, 48–66.
9. Moynihan. Edinburgh M. J., 1907, xxi, 228.
10. Robson. Brit. M. J., 1908, i, 425.
11. Rosenheim. Deutsche med. Wchnschr., 1907, xxxiii, 411.
12. Schloffer. Arch. f. klin. Chir., 1908, lxxxviii, 1.
13. Schreiber. Deutsche Arch. f. klin. Med., 1902, lxxvi, 122.
14. Senn. Principles of Surgery, 1895.
15. Strauss. Therap. d. Gegenw., 1909, xi, 313.
16. Tietze. Ergebn. d. Chir. u. Orthop., 1920, xii, 211.
17. Wilensky. Med. J. & Rec., 1932, 445, 446.
18. Wolfler and Lieblein. Deutsch. Chir., 1909.

STUDIES ON TUMOR METASTASIS

2. The Distribution of Metastases in Cancer of the Breast

SHIELDS WARREN, M.D., and EVA M. WITHAM, A.B., Boston
From the Laboratories of Pathology of the New England Deaconess and Pondville Hospitals

FEW malignant tumors show as wide variation in frequency and extent of metastasis as do the various carcinomata of the breast. On the one hand it is not infrequent to see a large colloid carcinoma of the breast of some years' duration without even involvement of the regional nodes, whereas in other cases a small, inconspicuous mass, apparently of short duration, will show the most bizarre and widespread metastases. At times, unfortunately, the first symptoms noted are those due to metastases, as a pathological fracture or intracranial pressure.

The present study is based on 162 autopsied cases of breast cancer selected from the New England Deaconess, Pondville, and Huntington Memorial Hospitals, and the House of the Good Samaritan. We have attempted to divide the cases of carcinoma into three groups on the basis of their histological appearance. The least differentiated is the carcinoma simplex, in which the tumor is growing in solid masses or cords of cells without alveolar formation. This tumor may be either scirrhous or medullary in its local lesion and metastases, with all gradations between. No significant variation has been detected in the behavior of the scirrhous and the medullary types, so therefore they are not separately considered in the present study. In general it may be said that our findings bear out the clinical observation that the larger and more bulky the local lesion the less extensive the distribution of metastases is apt to be.

More highly differentiated than the carcinoma simplex is the adenocarcinoma. In this form of tumor, under our classification, at least one-fourth of the tumor shows formation of definite alveoli. Here again the amount of stroma may vary greatly. Occasionally the metastases of such a tumor will show no alveoli.

A third, the most highly differentiated group, is the colloid carcinoma, characterized by the presence of a great amount of mucinous secretion, the absence of early metastases, a relatively limited distribution of late metastases, and as a rule very large local lesion.

In addition to these groups, which number 153 cases, were 5 cases of carcinoma that could not be classified, 2 cases of epidermoid carcinoma, apparently originating from Paget's disease, 1 lymphoblastoma, and 1 undifferentiated sarcoma, probably fibrosarcoma.

All the cases except the sarcoma occurred in females.

We have been able to confirm in part on this material Greenough's observations on the correlation of histological variation with prognosis. The time of metastasis is later in the more differentiated tumors, thus improving somewhat the prognosis as this holds true for the untreated cases and the cases showing metastasis before treatment (Table III). The presence of a fairly high proportion of metastases from tumors of all histological types does not permit too great reliance on grading. A wide variation of histological types is presented by the material. Our experience has been much more in accord with that of Reimann, and we feel that the wide variation in histology in the same tumor emphasized by Reimann, Ingleby, and others precludes any satisfactory histological grading. Even when the tumor presents a fairly uniform appearance, our attempts at grading have been unsuccessful. It may well be objected that an autopsy series is unduly weighted with cases of high malignancy. Certainly so far as distribution of metastases is concerned there is but little evidence of correlation between histological appearance and extent of metastasis. Size of the tumor cells has apparently little or no significance. However, the proportion of various grades corresponds fairly well with that found in our routine surgical material.

It must not be inferred from the foregoing that there is absolutely no correlation between

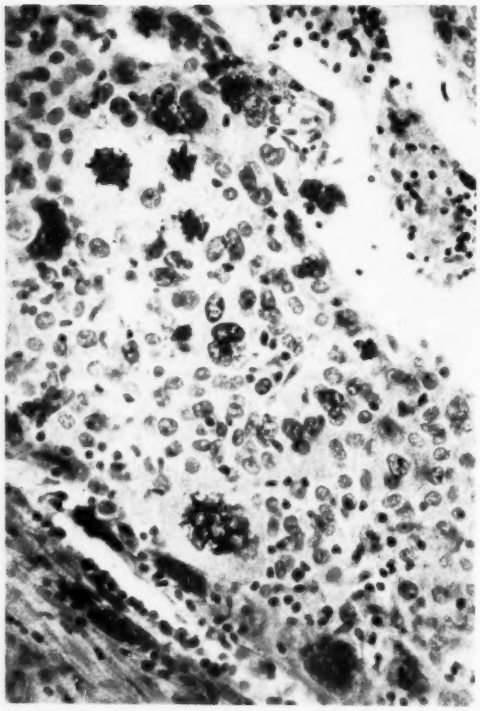


Fig. 1. Abnormal mitoses in carcinoma of the breast. Case 31-2984. × 200.

histological appearance of the lesion in the breast and prognosis or distribution of metastases. In certain cases of markedly anaplastic tumors, duration of life has been short and distribution of metastases has been wide. If any one factor stands out more definitely than others as a criterion of high malignancy in this group it is the occurrence of large numbers of abnormal mitotic figures. The frequency of mitotic figures of the normal type applies more to the local rate of growth than to the likelihood of metastasis. However, I have yet to see a tumor containing numerous mitoses of the type shown in Figure 1 fail to metastasize rather widely or kill promptly, as compared with the ordinary run of breast tumors.

As may be seen from Table I, operation was the predominant method of treatment in this group of cases. It is rather striking that 31 patients received either no treatment or palliative treatment, and 15 additional patients received only X-ray and 3 only radium treatment, which might well also be grouped in the palliative class.[1] Local recurrence was noted in 1 case of colloid carcinoma, 1 of unclassified carcinoma, 1 of epidermoid carcinoma, 1 of sarcoma, 30 (48 per cent) of adenocarcinoma, and 40 (46 per cent) of carcinoma simplex.

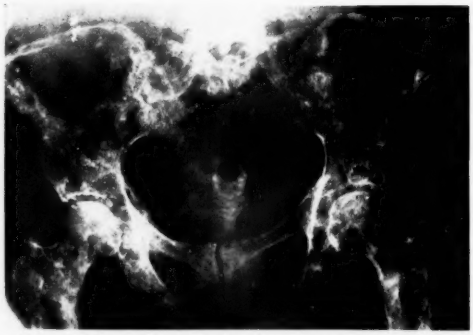


Fig. 2. X-ray of pelvis showing metastases from carcinoma of breast. Case 513.

When one considers that of 113 intensively treated cases, 74 showed local recurrence, it is at first glance a reflection on the types of treatment used. However, when it is remembered that this series is based on autopsied cases, the emphasis shifts, simply calling attention to the grave prognostic significance of this condition.

The average age at death of our cases, 57 years for the adenocarcinoma and the carcinoma simplex groups, fairly closely corresponds with that noted by other observers. The total duration from the onset of symptoms also corresponds quite closely with Wainwright's figures, being 3.2 years for the adenocarcinomata, 3.1 years for the carcinoma simplex group, and 3.1 years for the unclassified carcinomata. The colloid carcinomata and the epidermoid carcinomata have a much longer duration, 8 years and 6.5 years, respectively, though of course the series is too small to be significant. The delay between onset of symptoms and treatment in cases of adenocarcinoma and carcinoma simplex was approximately 10 months.

No other common cancer shows as wide distribution of metastases as does that of the breast. Only 8 cases failed to show metas-

[1]These cases were advanced when first treated.

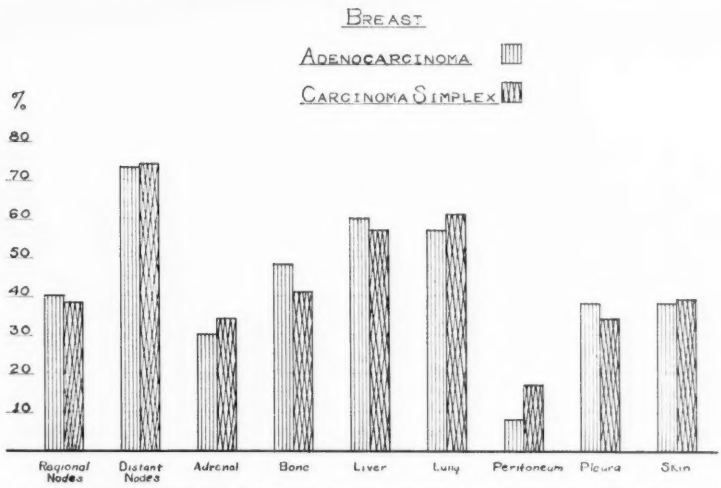


Fig. 3. Straight vertical lines show breast adenocarcinoma; crossed lines, breast carcinoma simplex.

tases at autopsy. The 154 cases with metastasis showed a total of 781 organs or tissues involved, an average of over 5 per case. There were actually far more metastases than these, as usually the metastases in a given site are multiple rather than solitary. When it is remembered that of these cases 113 had had radical operation with removal of the regional lymph nodes, in effect ruling out their most common site of metastasis, the number is even more striking. These radical operations of course explain the somewhat anomalous situation illustrated in both Table II and Figure 3, in which there are considerably fewer metastases to regional nodes than to distant nodes.

In this series of cases, the eye, the middle ear, the pineal gland, and the nasopharynx are practically the only tissues to be spared. The pituitary was involved once, a parathyroid once, the thyroid 4 times, one or both ovaries 15 times, the heart 7 times. By far the most frequent site of involvement is the distant lymph nodes. Following these in order of frequency are the lungs, liver, bone, regional lymph nodes, skin, pleura, and adrenal glands (Table II).

Not only is the distribution of metastases in these cancers of the breast particularly wide from the standpoint of space but in point of time as well. By study of the history, and of the gross and microscopic appearance of the metastases, we have attempted to estimate the time at which various metastases developed. The results are of course only approximate, but none the less of some interest. Thus in both treated and untreated cases of adenocarcinoma and carcinoma simplex, 129 metastases appeared within 1 year before treatment, 27 two years before, 2 three years, 4 four years, and 4 over four years (see Table III).

In the treated cases 295 metastases apparently developed in the first year after treatment, 141 within the second year, 48 within the third year, 7 within the fourth year, and 58 after 4 years, some of the latter developing, so far as could be determined, as late as 12 years after treatment. These late metastases are particularly apt to be single. Bone and brain, and lung are particularly frequent sites of late development, although the liver is also fairly frequently involved. Skin metastases are more consistently late in development than any other one group. The other breast was the site of metastasis in 20 instances, being involved within 2 years of the time of treatment in all but 2 of the 20 cases.

The adrenal glands were involved in 50 cases, far more frequently than any other of the ductless glands. This is due chiefly to the location of the glands or their lymphatic drain-

TABLE I.—CANCER OF THE BREAST

	Total cases	M	F	Average age, years	Average duration before treatment	Not stated, cases	Average duration after treatment	Total duration[1]	Average duration untreated	No treatment or palliative treatment, cases	Treated by operation, cases	Treated by radium, cases	Treated by X-ray, cases	Combined treatment, cases	With local recurrence, cases	With no metastases, cases
Adenocarcinoma	63	—	63	56.6	7.6 mos.	18	3.0 yrs.	3.2 yrs.	2.7 yrs.	13	27	2	2	19	30	2
Carcinoma simplex	87	—	87	57.6	11.5 mos.	25	3.0 yrs.	3.1 yrs.	2.3 yrs.	15	38	1	10	23	40	2
Colloid carcinoma	3	—	3	85	4 yrs.	1	6 yrs.	8 yrs.	6 yrs.	1	1	—	1	—	1	—
Lymphoblastoma	1	—	1	46	—	1	1.8 yrs.	1.8 yrs.	—	—	1	—	—	—	—	—
Carcinoma, undifferentiated or not stated	5	—	5	67	1.2 yrs.	1	2.46 yrs.	3.1 yrs.	N.S.	1	2	—	1	1	1	2
Epidermoid carcinoma	2	—	2	70	—	1	3.5 yrs.	6.5 yrs.	10 yrs.	1	—	—	—	1	1	1
Sarcoma, undifferentiated	1	1	—	65	1.5 mos.	—	6 mos.	0.6 yr.	—	—	—	—	1	—	1	1

[1]Total duration includes untreated cases as well as treated.

TABLE II.—DISTRIBUTION OF METASTASES

	Number of cases	Number of cases of breast cancer with metastases to								
		Regional nodes	Distant nodes	Adrenal	Bone	Liver	Lung	Peritoneum	Pleura	Skin
Adenocarcinoma	63	25	46	19	30	38	36	5	24	24
Carcinoma simplex	87	33	64	30	36	50	53	15	30	34
Colloid carcinoma	3	2	3	1	2	—	3	—	1	1
Lymphoblastoma	1	—	1	—	—	1	—	1	—	—
Carcinoma, not stated	5	1	2	—	1	—	1	—	1	2
Epidermoid carcinoma	2	—	—	—	—	—	1	—	—	—
Sarcoma, undifferentiated	1	—	—	—	—	—	—	—	—	—

age rather than their blood supply, shown by the fact that the thyroid with an equal or possibly more abundant blood supply was involved only 4 times. The right adrenal is more frequently involved than the left, and often the liver also shows metastases. Solitary metastases are the rule, and the medulla is a more frequent site than the cortex.

The spleen is not uncommonly (23 instances) a site of metastasis, although as a rule the metastases are small. This frequent involvement lends little credence to the assumed resistance of the spleen to the development of cancer. The capsule of the spleen is involved in peritoneal metastases fully as often as one would expect from its somewhat protected location.

We feel that we have noted most of the metastases to bone in this group of cases. In a number of instances where roentgenological examination had not been done fairly recently before, X-ray studies were made after, death.

Unfortunately, we have not distinguished in all instances between osteoclastic and osteosclerotic metastases. In general, the osteoclastic type predominates. By far the commonest sites are the lumbar vertebræ and the upper ends of the femora, although in some cases almost every bone in the body is involved (Fig. 2). In a study of the clinical records, it was noted that pain called attention early to the vertebral metastases, while usually femoral metastases were noted as a result of X-ray examination or pathological fracture.

TABLE III.—PROBABLE TIME OF DEVELOPMENT OF METASTASES BEFORE TREATMENT—(UNTREATED AND TREATED CASES)

	Adeno-carcinoma	Carcinoma simplex
Under 1 year	58	71
1–2 years	19	8
2–3 years	—	2
3–4 years	1	3
More than 4 years	—	4
Not stated	5	23

We believe that the great majority of bone metastases are hæmatogenous. Those portions of bone with abundant blood supply are usually involved, and the wide sinusoids of the marrow spaces offer ideal sites for deposition of tumor emboli. Moreover, of 69 cases with metastases to bone, 41 showed pulmonary metastases, thus providing easy and direct access to the systemic circulation. Evidence is fairly strong that minute viable tumor emboli may pass through the pulmonary circulation without establishment of metastases in the lungs.

Material suitable for study of the mode of transmission of metastases was not obtained in most of our cases. However, in several, detailed studies were made of all tissues intervening between the primary tumor and involved axillary nodes. We found lymphatic permeation to occur in only one far advanced case with extremely widespread metastases. The evidence for embolic distribution is far stronger.

Distribution from the primary growth by way of the blood stream is rare, although at times clearcut invasion of vessels may be seen in the primary cancer, particularly in the more anaplastic tumors. Usually when dissemination occurs by the blood stream the metastases in the lungs are the sources of tumor emboli.

TABLE IV.—PROBABLE TIME OF DEVELOPMENT OF METASTASES AFTER TREATMENT

	Adeno-carcinoma	Carcinoma simplex
Under 1 year	111	184
1–2 years	61	80
2–3 years	21	27
3–4 years	18	19
More than 4 years	27	31

SUMMARY AND CONCLUSIONS

1. The distribution of metastases in 162 autopsied cases of breast cancer is reported.

2. In general, histological appearance is not related to the extent of metastases.

3. Metastases of breast cancers average over five per case.

4. Practically every organ or tissue of the body has been noted as a site of metastasis.

5. Metastasis occurs usually by emboli in lymphatic channels.

6. Direct blood borne metastasis occasionally is seen.

7. Most osseous metastases are hæmatogenous.

REFERENCES

1. GREENOUGH, R. B. J. Cancer Research, 1925, ix, 453.
2. INGLEBY, H. Arch. Path., 1929, viii, 653.
3. LANE-CLAYPON, J. E. Brit. Public Health Rep., 1926, No. 32.
4. REIMANN, S. Arch. Path., 1929, viii, 803.
5. WAINWRIGHT, J. M. Am. J. Cancer, 1931, xv, 2610.

CLINICAL SURGERY

FROM THE GASTRIC SERVICE OF THE MEMORIAL HOSPITAL, NEW YORK

THE JIANU GASTROSTOMY

GEORGE T. PACK, M.D., NEW YORK

THE purpose of a gastrostomy is to afford an inlet for food and liquid in cases of inflammatory or neoplastic obstruction in the œsophagus or cardiac end of the stomach. A permanent gastrostomy should fulfill the following requirements: There should be no leakage of food, liquids, or gastric juice from the stoma in order to avoid excoriation of skin or the necessity for wearing a dressing. The stoma of a gastrostomy should be controlled by a sphincter or valve. There should be no necessity for constantly wearing a tube, which needs be inserted only at the time of feeding. The gastrostomy should be lined by mucosa as granulation tissue is unsuitable for a permanent fistula. The operation should be so planned that the food enters at the fundus rather than at the pyloric end of the stomach. It is highly desirable that the gastrostomy permits the ingestion of semisolid food such as ground meat as well as liquids. The possibility of resection of the lower end of the œsophagus in patients with suitable œsophageal cancers, which lend themselves to successful extirpation, should be considered and a type of gastrostomy selected which may aid in the reconstruction of an œsophagus. Another desideratum is that the canal extending from the stomach to the skin be as long and narrow as possible so that the feeding tube fits snugly when it is introduced; furthermore, the canal itself should bend and thereby prevent the regurgitation of digested food through the stoma.

There are conflicting opinions about the advisability of performing gastrostomy for inoperable carcinomata of the œsophagus and cardia. It has been asserted by some physicians that life is not worth while if food must be ingested unnaturally through a gastrostomy rather than by normal mastication and deglutition. A well designed and functioning gastrostomy enables the patient with cancer of the œsophagus or cardia to live

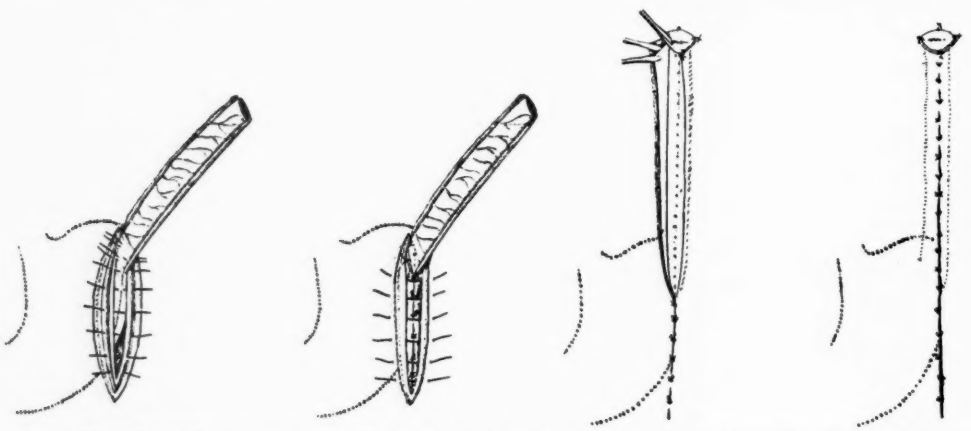


Fig. 1. The original Jianu gastrostomy. The fundus is anchored to the abdominal incision. Note the continuation of the skin incision superiorly onto the thorax in order to imbed the gastrostomy tube. (Jianu, A. Deutsche Ztschr. f. Chir., 1912, cxviii, 383.)

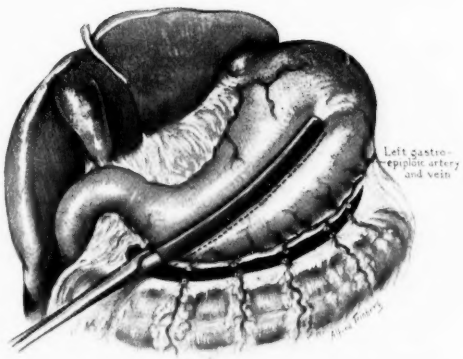


Fig. 2. Jianu gastrostomy. First step. Ligation and division of gastrocolic omentum with preservation of left gastro-epiploic artery. Right gastro-epiploic artery doubly clamped, divided, and ligated at pyloric end of stomach. Lower third of stomach to be severed between two long soft clamps (lower clamp not illustrated in order to show line of incision). Another small clamp is placed gently across base of flap at fundus to avoid soiling of operative field.

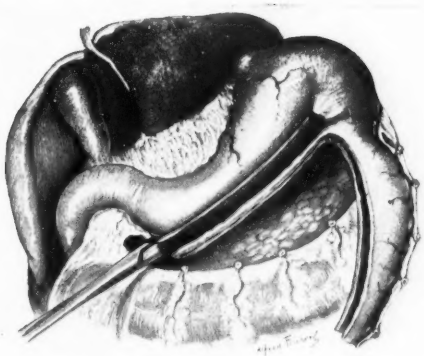


Fig. 3. Jianu gastrostomy. Second step. Semidiagrammatic sketch to show the construction of the gastrostomy tube. An inner Connell suture and an outer continuous Lembert suture close the stomach and the tube.

longer and to suffer less. The gain in weight after gastrostomy is convincing evidence of the value of this procedure. The presence of a gastrostomy does not prevent the intake of fluids by mouth if that be possible. In fact, many œsophageal cancers become pervious again and permit the patient to drink liquids after a gastrostomy has been performed, because the infection of the cancer has subsided and there is less dilation of the œsophagus above the stenosing lesion. Bouginage as an alternative of gastrostomy has certain obvious disadvantages; it cannot always be employed and is seldom successful unless the carcinoma is situated in the upper half of the œsophagus. Bouginage is painful and attended by the dangers of perforation or hæmorrhage. Furthermore it must be repeated at frequent intervals. Retrograde bouginage through the gastrostomy is safer and more successful for

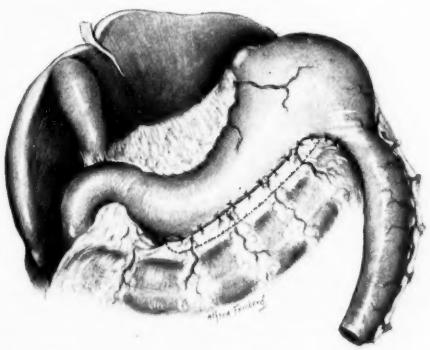


Fig. 4. Jianu gastrostomy. Third step. Reconstruction of stomach after formation of tube from greater curvature. The gastrocolic ligament is re-attached to the stomach above the suture line. The tube is 8 to 9 inches in length.

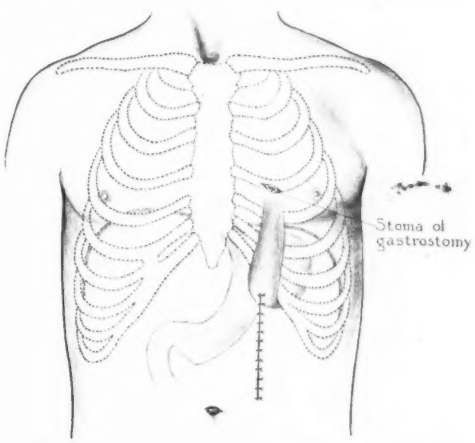


Fig. 5. Jianu gastrostomy. Fourth step. Location of incision for permanent gastrostomy in order to secure valve-like control against leakage by pressure against costal margin. If anastomosis to œsophageal stump is planned, the incision should be in mid-epigastrium, as the stoma then can be placed much higher. Abdominal wound completely closed. The tube emerges through muscle and fascia, then is drawn subcutaneously to the incision on chest selected for the stoma.

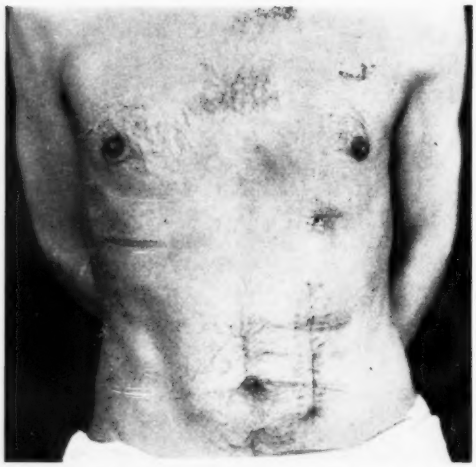


Fig. 6. Photograph of patient with Jianu gastrostomy. The stoma could have been placed on a level with the nipples if an œsophagectomy and plastic restoration had been considered. There is no leakage of gastric contents and no excoriation of skin surrounding the stoma. This patient has regained his normal weight.

Fig. 7. Radiogram of stomach after introduction of barium sulphate through Jianu gastrostomy. The rubber catheter for feeding is in place. The goose-neck is not completely visualized but its direction under and over the costal margin can be seen. The base of the tube is continuous with the fundus of the stomach.

stenosing carcinomata of the cardia and terminal œsophagus than peroral dilatation. Another argument supporting the advantage of gastrostomy over bouginage is the danger of dissemination of the carcinoma by the trauma incident to forceful dilatation. The unsatisfactory end-results and high mortality rate generally reported for gastrostomies can be attributed to the great delay before the operation is performed in the average case. The surgeon should anticipate complete obstruction of the œsophagus or cardia and perform a gastrostomy before the patient becomes so emaciated and dehydrated as to be a poor operative risk.

According to my count at least 36 different methods of gastrostomy have been devised since the operation was first suggested in 1837 by Eggebert. The earliest record of its use was in 1841 when Blaudlot performed this operation on a dog. In 1843 it was successfully and independently done in humans by Sédillot and Nélaton. A study of the evolution of gastrostomy reveals that only four different procedures are utilized. These are elaborated in some detail in the accompanying chart. The use of a simple gastric cone obtained from the anterior wall of the stomach as described by Sédillot, Frank, and others, seldom fulfills the requirements of a successful gastrostomy even when the various procedures to secure sphincteric control are employed. It can be used only when the stomach is quite atonic and relaxed and in the majority of cases the gastrostomy is not water-tight.

The Senn operation, in which the cone of the anterior stomach wall is inverted by successively larger and wider pursestring sutures is probably the most successful of these simple types, as the inverted cone functions as a valve. The well known Witzel method is in general use for jejunostomy, but it is inferior to the Marwedel technique because it tends to occlude the lumen of the stomach or jejunum. The Marwedel gastrostomy resembles the Witzel in general principle, except that after the rubber tube is introduced through an initial puncture wound and pursestring suture, the stomach wall is not grooved entirely around the catheter but a linear incision is made through the seromuscular coat of the stomach or jejunum and the catheter is buried in the submucosa with the seromuscular layer sutured over it; in this type the gastrostomy canal and the rubber catheter is submucosal in location. The Witzel and Marwedel gastrostomies are not suitable for permanent fistulæ.

The substitution of another hollow organ such as the jejunum or transverse colon to be used as a gastrostomy tube is impractical, because the operation is difficult and frequently unsuccessful and the mortality rate is very high in marked disproportion to the safety of the simpler varieties of gastrostomy. This procedure should never be done if the only indication for the gastrostomy is to feed the patient. The only possible indication for this technique is when resection of the œsophagus for carcinoma is planned and the surgeon wishes to attempt restoration of the continuity of the alimentry tract by reconstruction of a tube to serve as an œsophagus. When the jejunum is used, it necessitates the resection of a loop of this intestine, re-anastomosis of the jejunum, resection of the œsophagus, implantation of the jejunal loop into the stomach as well as to the distal end of the œsophageal stump. In order to pull up such a loop as high as possible the mesentery must be cut from the oral end, extending parallel to the intestine, care being used to preserve the vascular arches close to the intestine. At the inner end of this isolated jejunum there remains a narrow mesenteric pedicle which maintains the blood supply to the intestine, although gangrene frequently supervenes.

The most satisfactory gastrostomy is the type which is based on the construction of a tubed pedicled flap from the anterior wall or greater curvature of the stomach. Depage in 1901 first performed such a gastrostomy. He outlined a rectangular flap or trap-door with the incision entirely through the gastric wall on three sides of the rectangle, the base being left at the lesser curvature of the stomach. This full thickness plastic flap is converted into a tube by continuous mucosal and seromuscular sutures; this tube or goose-neck is lined with gastric mucosa and opens into the lesser curvature of the stomach. Under novocain anæsthesia, a 3-inch vertical incision is made under the left costal margin. The anterior gastric wall is easily delivered through this small mid-rectus incision, and the construction of the plastic tube performed entirely without the abdominal cavity. It may be used when the stomach is immobile because the length of the flap permits its extension to the skin. It affords a valve lined by mucosa. It has an abundant blood supply and there is no danger of necrosis of the extremity of the flap. It extends upward to the skin and because of its attachment to the lesser curvature food and gastric juice do not regurgitate.

Janeway, in 1913, modified this procedure by constructing the flap with the base at the greater curvature. The advantage he claimed was that the suture line is placed on the upper surface of the tubular canal, thus subjecting it to less strain from the weight of the filled stomach. This objection to the Depage gastrostomy is not a valid one inasmuch as the stomach is seldom overdistended until the wound is entirely healed. Furthermore, the Depage gastrostomy has a better blood supply from the lesser curvature than the Janeway gastrostomy can secure from the greater curvature of the stomach. An additional advantage the Depage has over the Janeway gastrostomy is that the location of the base of the tube is at the lesser curvature rather than at the greater curvature, thereby insuring less regurgitation. If the body of the stomach (corpus ventriculi) is situated high under the costal margin or is retracted upward by a carcinoma of the cardia and lesser curvature, the Janeway gastrostomy is preferable to the Depage because only the greater curvature may be low enough to serve as a base for the plastic tube if its direction (inward and downward) is maintained.

Hirsch, in 1911, devised a gastrostomy similar to the Depage except that the rectangular flap was very long and situated obliquely across the anterior gastric wall with the base near the cardia and the free end near the pylorus. This operation was performed only on dogs and apparently never was used on a human subject. Although Hirsch stated that several large arterial branches from the left superior gastric artery enter the base of the flap, it is very likely that this flap has a poorer blood supply than either the Depage or the Janeway type of gastrostomy.

Amza Jianu, a Roumanian surgeon of Bucharest, devised a gastrostomy in 1912 which offered the advantages of serving not only as a feeding tube but was also suitable as the first step in the reconstruction of a new œsophagus. In Jianu's method, the greater curvature of the stomach is converted into a plastic tube hinging at the fundus. Jianu performed this operation solely on dogs and human cadavers. Roepke was the first surgeon to do a Jianu gastrostomy on a living human subject. This method has found favor with certain American surgeons, Willy Meyer in 1913 and Horsley at a later date both advocating its use. The procedure is not a difficult one and the danger to the patient is slight. It possesses all the advantages of the ordinary tubed gastrostomy and in addition may serve as the lower half of a reconstructed œsophagus in the event that the surgeon later wishes to attempt an œsophagectomy. This gastrostomy

may be done in patients with inoperable œsophageal carcinomata, for which no further operative procedures are planned. By so doing, the surgeon acquires the necessary technical experience, so that in selected cases in which œsophagectomy is feasible, the first stage or construction of a long gastrostomy tube may be done with a great chance of success.

TECHNIQUE

The operation utilizes the greater curvature of the stomach to form a long pedicled tubed flap with the base at the fundus. If the gastrostomy is intended for feeding purposes only, a high left mid-rectus incision is done; if the surgeon plans to do an œsophagectomy and wishes to utilize the tube flap in the reconstruction of the œsophagus, then a midline epigastric incision is done, the incision being started as high as the xiphoid cartilage. The stomach wall is exposed by the incision. The gastrocolic ligament is divided at a distance of about 1 inch from the greater curvature, with care to preserve the left gastro-epiploic artery which will serve as the main blood supply of the future gastrostomy tube. The part of the gastrocolic ligament attached to the transverse colon is kept intact as it may be used to suspend the transverse colon and in some instances to protect the suture line of the stomach (Fig. 4). The gastrosplenic ligament is also severed between two ligatures.

The stomach is now clamped longitudinally along the greater curvature with long soft rubber-covered clamps beginning at the antrum and extending high onto the fundus (Fig. 2). Horsley places these clamps midway between the greater and lesser curvatures, but it is my practice to extend them only one-third of the way up from the greater curvature in order to leave more normal stomach. At the base of the proposed flap on the fundus, a short rubber covered clamp is placed gently in a transverse position in order to isolate this segment and to prevent leakage of gastric contents during the operation. This clamp should not be placed too tightly or it might interfere with circulation. The right gastro-epiploic artery is doubly clamped, severed, and doubly ligated at the distal end of the stomach. It is the left gastro-epiploic artery upon which the circulation of the flap is dependent.

The incision is made between the two clamps and extends from the antrum to the fundus. The incision is carried through both the anterior and posterior stomach walls, the leaves of which are sutured to construct a gastrostomy tube with a lumen at least 1 inch or more in diameter (Fig. 3). I have employed two layers of sutures, the inner a Connell suture of chromic catgut and a continuous serosal Lembert suture of silk.

If the gastrostomy is to be used only for feeding purposes, the gastrocolic ligament may then be sutured over the suture line in the stomach particularly at the angle of reflexion of the stomach onto the base of the tubed flap. It suspends the transverse colon and furthermore furnishes a defensive guard for the gastric suture line. On the contrary, if the stoma of the gastrostomy is to be placed high on the chest wall or if the tube is delivered through a midepigastric incision, the weight of the colon exerts too much tension on the stomach when the gastrocolic ligament is sutured to this organ.

In his original article, Jianu described the anchorage of the stomach to the upper part of the abdominal wound by interrupted Lembert sutures. This procedure tends to prevent sacculation of the fundus at the base of the tube and to avoid the formation of an hour glass stomach. It lessens considerably the tension on the tube caused by the weight of a distended stomach. The later authors do not stress this step sufficiently and many of them have probably not anchored the stomach, as outlined by Jianu.

After the anterior and posterior edges of the stomach are sutured together and the suture is continued at the flap to form a closed tube, this goose-neck is gently drawn out through the upper end of the abdominal incision and placed upward over the chest wall in order to judge how high it can extend. The tube frequently measures 8 to 10 inches in length. A small transverse incision about 1½ inches long is made, after the site of the stoma has been selected in this way. The surgeon then burrows through the subcutaneous tissues from this skin incision down over the ribs until a Kelly clamp enters the subcutaneous plane of the abdominal incision. This subcutaneous channel is dilated until it is much larger than the tube, otherwise it may contract on healing and constrict the tube sufficiently to interfere with its blood supply. The surgeon introduces the clamp through the incision for the stoma, grasps with this clamp the extremity of the gastrostomy tube and draws it through this subcutaneous channel until the end of the tube reaches the incision in the skin. Infection of the subcutaneous channel may be avoided by temporarily inverting the tip of the goose-neck of tube by two sutures, or the end of the tube may be covered by a finger cot or a rubber condom. After the tube has been delivered through the

incision for the stoma, it may be left unopened for 24 to 48 hours at which time the occluding sutures are removed.

There is considerable risk of sacculation of the intra-abdominal portion of the tube and subsequent difficulty in feeding, if the tube is left slack and is not pulled up snugly. The blood supply runs in a longitudinal direction; therefore any suture in the extremity of the tube should be placed in this same direction otherwise it may interfere with the blood supply of the tip with resultant ischemic necrosis.

In the original Jianu operation on dogs, the abdominal incision was extended upward onto the chest as high as the tube would reach. Then the skin incision was sutured over the tube (Fig. 1). Roepke, Willy Meyer, Horsley, and others who have employed the modified Jianu gastrostomy have all dispensed with this added incision and delivered the tube through a subcutaneous channel instead (Fig. 5). The danger of infection is probably greater with the number of sutures required for the long skin wound of Jianu than it is by burrowing the tube through a long subcutaneous channel.

The abdominal wound is closed in layers. The peritoneum and split rectus muscle are closed by continuous plain catgut sutures. The fascia is closed by interrupted chromic catgut sutures, which fit snugly but not too tightly around the tube. The skin is completely closed preferably by interrupted sutures in order to allow for drainage if it is necessary during the healing of the wound. Thus the tube extends through the peritoneal, muscular and fascial layers but does not extend through the skin of the abdominal incision. A small drain is placed subcutaneously at the lower end of the abdominal wound.

The completed gastrostomy is ideal in every respect. The stoma is situated so high above the stomach that regurgitation of food and gastric juice never occurs. The tube is bent upward over the costal margin or over the xiphoid cartilage and in so doing obstructs the lumen sufficiently to serve as a very good valve and in this way also prevents the regurgitation of food through the gastrostomy. The blood supply is adequate and even the extremities of a very long tube will never suffer from ischæmia. The rectus muscle may also serve as a sphincter. The tube has a much larger lumen than occurs in the Janeway or Depage gastrostomies, and on this account it is possible to give semisolid food such as ground meat. Puréed vegetables and ground meat can later be given through this gastrostomy, by using a small grease gun for the introduction.

A rubber catheter, No. 12 or 14 French, is left in the gastrostomy during the first 10 days. Water and peptonized milk are given immediately after the operation and the liquid and semisolid diet increased quickly until the patient is soon on a well balanced, high caloric diet.

EVOLUTION OF GASTROSTOMY

A. Elevation of simple cone from anterior wall of stomach. Sédillot (1846).
   1. Use of rectus muscle as a sphincter for gastrostomy cone. Girard (1888), V. Hacker (1890). Jaboulay (1894), Terrier and Gosset (1902).
   2. Traction of gastric cone through oblique canals between muscles, fascia, and subcutaneous tissues to give sphincteric control. Hahn (1890), Sabanieff (1890), Hartmann (1891), Frank (1893).
   3. Rotation of gastric cone to form a valve for the gastrostomy. Ullmann (1894), Souligoux (1902).

B. Canalization of gastric wall.
   1. Invaginated gastric cone by series of pursestring sutures. Senn (1896), Fontan (1896).
   2. Intramural canal not lined by mucosa.
      a. Puncture wound and inversion of sound or rubber catheter by plication of stomach wall with sero-serosal sutures. Witzel (1891), Kocher (1902).
      b. Puncture wound and burial of sound or rubber catheter in submucosal canal by suture of seromuscular coats. Marwedel (1896).

C. Substitution of other hollow viscera as tubes between stomach and skin.
   1. Isolated, pedicled segment of jejunum. Roux (1907), Wullstein, Frangenheim (1911), Lexer (1911).
   2. Isolated pedicled segment of transverse colon. Kelling (1911), Vulliet (1911).

D. Construction of tubed pedicled flaps from gastric walls.
   1. Tubed flap with base at lesser curvature. Depage (1901).
   2. Tubed flap from anterior stomach wall with free end near pylorus and base at cardia and fundus. Hirsch (1911).
   3. Tubed flap by severance of greater curvature with base at fundus. Jianu (1912).
   4. Tubed flap of anterior stomach wall with base at greater curvature. Janeway (1913).

SUMMARY

The evolution of the methods of gastrostomy is discussed. The indications, advantages, and technique of the Jianu gastrostomy are presented. The Jianu operation utilizes the greater curvature of the stomach to form a long tubed flap with the base at the fundus. This tube may be used not only for a gastrostomy but also as the initial step in the reconstruction of the œsophagus.

BIBLIOGRAPHY

1. Blaudlot. Traité analitique de la digestion. Paris, 1843.
2. Depage. J. de chir., 1901–1902, 1, 715; Tr. 16th Cong. French Surgeons, Paris, 1903.

3. Eggeberg *in:* L. H. Petit. Traité de gastrostomie. Paris, 1879.
4. Fontan. Une nouvelle opération de gastrostomie. 10me Cong. franç. de. chir., Paris, 1896.
5. Frangenheim. Zur Frage der Oesophagusplastik. Arch. f. klin. Chir., 1911, xlv, 3.
6. Frank, S. Eine neue Methode der Gastrostomie bei einem Carcinoma œsophagi. Wien. klin. Wchnschr., 1893, vi, 231.
7. Girard. Neue Methode der Gastrostomie mit Sphinkterbildung. Cor.-Bl. f. Schweiz. Aerzte., 1888, xi, 345.
8. Hahn. Eine neue Methode der Gastrostomie. Zentralbl. f. Chir., 1890, Nos. 193–195.
9. Hartmann. Note sur la gastrostomie dans le cancer de l'oesophagus. Bull. Soc. anat., 1891, p. 117.
10. Hirsch, Maximilian. Plastischer Ersatz des Oesophagus aus dem Magen. Zentralbl. f. Chir., 1911, xxxviii, 1561–1564.
11. Horsley, J. Shelton. Surgery of the Stomach and Small Intestine. pp. 151–153. New York: D. Appleton and Co., 1926.
12. Jaboulay. Procédé pour practiquer la gastrostomie et la cystostomie. Gaz. hebd. de méd., 1894, p. 89.
13. Janeway, Henry H. The relation of gastrostomy to inoperable carcinoma of the esophagus. J. Am. M. Ass., 1913, lxi, 93–95.
14. Jianu, Amza. Gastrostomie und Oesophagoplastik. Deutsche Ztschr. f. Chir., 1912, cxviii, 383–391.
15. Kelling. Oesophagoplastik mit Hilfe des Quercolon. Zentralbl. f. Chir., 1911, Sept.
16. Martin, H. E., and Watson, W. L. The original Janeway gastrostomy. Surg., Gynec. & Obst., 1933, lvi, 72–78.
17. Marwedel. Zur Technik der Gastrostomie mit Krankenvorstellung. Beitr. z. klin. Chir., 1896, xvii, 56.
18. Meyer, Willy. Oesophagoplasty. Ann. Surg. 1913, lviii, 289–295.
19. Quick, D., and Martin, H. E. The most common methods of gastrostomy with the report of a modified technique of the Janeway method. Surg., Gynec. & Obst., 1928, xlvi, 426.
20. Roepke, W. Ein neues Verfahren fuer die Gastrostomie und Oesophagoplastik. Zentralbl. f. Chir., 1912, xxxix, 1569–1571.
21. Roux. L'œsophago-jejuno-gastrostomose: nouvelle opération pour retrécessement infranchisable de l'œsophage. Semana méd., 1907, pp. 37–40.
22. Sédillot. De la gastrostomie fistuleuse. Acad. de Sci., 1846, p. 222.
23. Senn, Emanuel J. Gastrostomy by a circular valve method. J. Am. M. Ass., 1896, xxvii, 1142.
24. v. Hacker. Ueber die Verwendung des musculus rectus abdominis zum Verschlubs der kuenstlichen Magenfistel. Wien. klin. Wchnschr., 1890.
25. Witzel. Zur Technik der Magenfistelanlegung. Zentralbl. f. Chir., 1891, xviii, 601.

THE TRANSVERSE INCISION IN THE UPPER ABDOMEN

WILLARD BARTLETT, M.D., F.A.C.S., AND WILLARD BARTLETT, JR., M.D., SAINT LOUIS

OUR interest in the transverse incision in the upper abdomen was stimulated largely by dissatisfaction with the difficulties inherent in the more commonly used vertical incision. The latter is fundamentally unsuited to too many patients requiring operations on the extrahepatic biliary system, 40 per cent of those reported here being grossly obese. That one is working against the patient's efforts becomes obvious as soon as an inhalation anæsthetic is administered and the patient's attempts to obtain adequate pulmonary ventilation in the face of decreased vital capacity bear witness to the physiological and anatomical handicaps under which he lives. Though there is not a general realization that increased intra-abdominal tension and decreased vital capacity go hand in hand, all changes in intrathoracic or intra-abdominal tension being transmitted through the diaphragm, it is easy to predict during incision in which case proper closure will be easy and in which it will be difficult or impossible. When one has finally accomplished accurate closure of all layers in a half-suffocated patient, whether the difficulty in gaseous exchange be in the pulmonary or in the internal respiration, there is little comfort in the immediate outlook, for such patients usually have a stormy postoperative course with slight, clinically discernible cyanosis and persistent vomiting. We have had them report sudden relief after a sensation of "something giving way." In one patient, Miss M. B. (October, 1931), efforts to close the posterior aponeurosis and peritoneum were finally abandoned, the omentum brought up to the wound, and the rectus muscle (which had been split in its inner third) was closed as the deepest layer, followed by the anterior aponeurosis and skin. She did not vomit following operation, showed none of the characteristic dusky color and anxious expression of those in whom the posterior aponeurosis is approximated, and seemed, indeed, to have been under no greater strain than a slim person would have been after appendectomy through a McBurney incision. Re-examination in March, 1933, showed deviation of the umbilicus 2 centimeters to the left (nerve injury), but a perfectly firm abdominal wall without transmission of impulse on cough or strain or bulging on sitting up. We are convinced that, by failing to close the posterior aponeurosis in her case, we simply anticipated the tearing through of sutures that must occur shortly after operation if the patient is to recover the pre-operative physiological status.

We were unwilling to face indefinitely a situation so unsatisfactory in immediate results and in its remote implications of hernia and adhesions. All true hernias through incisions, as contrasted with weak abdominal walls due to nerve injury, probably have their origin during postoperative convalescence in the hospital due to giving way of the suture in the posterior aponeurosis and peritoneum. Sprengel is quoted by Singleton as having observed this in those who died shortly after operation and one of us (W. B., Sr.) has repeatedly seen this. For these reasons we turned to the transverse incision in the upper abdomen as a truly anatomical and physiological procedure. We are so impressed with its value and find its drawbacks so few that we hope to encourage others to use it. The literature on the subject is small enough that a perusal of the original articles is well worth while. All contributors list very much the same dissatisfaction with the vertical incision and their unwillingness to give up the transverse incision once they have become familiar with its use. Sprengel, Perthes, and Bakes, in Germany, gave the greatest impetus to the procedure as a method of approach to the upper abdominal viscera; though Maylard in England was perhaps the first to perform complete transverse division of all structures, his report in 1907 is concerned with operations below the umbilicus. Clifford Collins, in the United States, was attempting to solve the problem of a truly anatomical approach to the gall bladder and extrahepatic bile ducts and his contribution in 1908 has not received the attention that, historically, it deserves.

ANATOMY OF ABDOMINAL WALL ABOVE THE UMBILICUS

The articles by Maylard, Southam, and Moschcowitz go very fully into the anatomy and physiology of the anterior abdominal wall above the umbilicus and only a brief emphasis will be laid on certain points important to our purpose.

Muscles and fascia. The "flat" muscles (external oblique, internal oblique, and transversalis), the fibers of which are predominantly transverse in direction, are inserted into the linea alba by two fibrous aponeuroses one of which passes anterior to the rectus muscle, the other

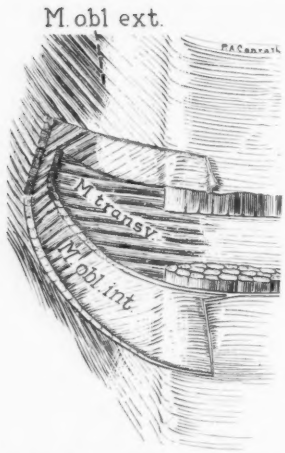


Fig. 1. Anatomical details of the right lateral abdominal wall just above the level of the umbilicus.

posterior to the rectus (Fig. 1). The anterior aponeurosis is formed by the fusion of the fascia of the external oblique with the anterior lamella of the fascia of the internal oblique. The posterior aponeurosis is formed by the fusion of the posterior lamella of the fascia of the internal oblique with the transversalis fascia. The anterior and posterior aponeuroses fuse to form the linea alba which is a thick, single layer structure. The correct physiological-anatomical conception is not of anterior and posterior layers of the "sheath of the rectus," but of *anterior and posterior* aponeuroses of the lateral abdominal muscles, shifting the emphasis to their origin and to the transverse direction through which their pull is exerted on the linea alba. McArthur emphasized the rôle of the transversalis as a muscle of respiration, and Sloan found that it requires a pull of 30 to 50 pounds to approximate the aponeuroses when divided vertically with the patient only lightly anæsthetized; when, however, the aponeuroses were divided transversely only a negligible force was necessary to reunite them. This fact was confirmed both by Singleton and by Mason.

Each rectus muscle is firmly attached to the anterior aponeurosis by lineæ transversæ, one at about the level of the umbilicus, a second opposite the xiphoid, a third approximately between these points, and a fourth below the umbilicus. The lineæ transversæ do not often extend through more than half the thickness of the muscle, so that the posterior aspect of the rectus is only loosely attached to the posterior aponeurosis. This division of the rectus into segments is further emphasized by the distribution of the nerves in the muscle.

Nerve supply. The rectus muscle is innervated by the fifth to the twelfth thoracic nerves, the oblique and transversalis muscles by the seventh to twelfth thoracic and the ileohypogastric and ileo-inguinal branches of the first lumbar (18). The intercostal nerves enter the abdominal wall at the costal border, lying between the internal oblique and the transversalis muscles. According to Quain (14), a very fine network of filaments runs mesially at this level to give the parietal peritoneum its sensory and trophic innervation. The intercostal nerves continue medially approximately parallel to the fibers of the transversalis to pierce the posterior aponeurosis at the lateral border of the rectus. Each nerve then divides into two branches: (1) the larger proceeds medially, lying posterior to the rectus, as far as the midline of the muscle which it enters, breaking up into a plexiform arrangement and giving off an anterior cutaneous branch which pierces the muscle anteriorly and does not appear to cross the midline (Southam); (2) the smaller branch pierces the outer half of the rectus, which it innervates. The seventh intercostal nerve terminates in the region of the xiphoid, the tenth at approximately the level of the umbilicus. In the operative fields of the upper abdomen, therefore, one will ordinarily encounter the eighth and ninth intercostal nerves and, if working lateral to the rectus muscle or near the umbilicus, may encounter the tenth. A vertical incision at the lateral border of the rectus will, therefore, destroy the entire nerve supply of that muscle to the corresponding level; one splitting the rectus lateral to its central line will destroy the innervation of its medial half. This was found to be the fact by Southam and other writers. Vertical incisions through the anterior aponeurosis with lateral retraction of the muscle and incision of the posterior aponeurosis in its inner third did not result in atrophy of the rectus.

Blood vessels. According to Maylard, the blood supply of the anterior abdominal wall is chiefly longitudinal and the most important vessels are the superior epigastric (O. T., internal mammary) and the inferior epigastric (O. T., deep epigastric) which, above the umbilicus, lie on the posterior aponeurosis immediately posterior to the rectus; they anastomose freely. More laterally, the blood vessels and lymphatics run more transversely in a course similar to that of the intercostal nerves. The linea alba is avascular and is almost devoid of lymphatics.

LATER DEVELOPMENT OF UPPER ABDOMINAL INCISIONS

Since the appearance of the original papers in the English, German, and American literatures, there have been further contributions of various personal experiences with upper abdominal incisions, transverse in part or in whole. No serious adverse criticism of the plan has come to our attention. Modifications have been suggested from time to time with a view to overcoming the minor difficulties of the procedure which are encountered by everyone on first acquaintance with it. In general, those who have contributed to the subject have followed one of two plans, differentiated chiefly by their management of the rectus muscles.

1. *Direct transverse division of all layers, including the rectus.* Farr, 1915; Quain, 1920; Moore, 1922; and Southam, 1924, have followed the plan of Maylard, cross-cutting the rectus without preliminary hæmostatic and fixation sutures. Meyer, 1915; Moschcowitz, 1916; and Jones and McClure, 1930, have inserted such sutures before cutting the muscle as in Perthes' modification of Sprengel's incision. The former group feels that the rectus retracts only segmentally and to so slight an extent that an adequate repair is made as part of the closure of the anterior aponeurosis. Farr, indeed, measured 150 cases and reported that 1 centimeter of muscle invariably projected beyond the suture line in the aponeurosis. The latter group emphasizes the hæmostatic rather than the fixation purpose of the preliminary muscle suture.

2. *Transverse division of posterior aponeurosis without cross-cutting rectus.* McArthur, 1915, presented a muscle splitting incision for operations on the gall bladder like that suggested by Collins for cholecystostomy. The method of Sloan, 1927, consists of vertical incisions in both anterior aponeuroses, lateral retraction of both recti, and transverse division of the posterior aponeuroses extending through the linea alba. Singleton, 1931, reported a modification of Sloan's method, using a transverse incision through skin and fat and omitting the vertical incision in the anterior aponeurosis on the left; the recti are retracted laterally, as by Sloan. Tate Mason, 1929, goes on the theory, for which there is considerable evidence, that a short incision is less apt to be followed by hernia than a long one, and makes a left, paramedian, vertical incision from the xiphoid almost to the umbilicus and a shorter right, paramedian vertical incision extending below the umbilicus; the lower end of the first incision and the upper end of the second are joined by a transverse incision extending through the linea alba and both recti are retracted laterally; the transverse incision is overlapped in closure.

3. Particularly abroad, there have been efforts made to get more exposure than obtained through the classical transverse incision of all layers, but they have not found favor in this country. Willy Meyer, who in 1915 reported using the straight transverse incision for the exposure of the stomach and duodenum, in 1917 favored the Perthes rectus flap operation (22 cases) for the gall bladder and bile ducts. He had also used the Koenig-Kehr flap operation (3 cases). His illustrations show also a downward extension of the lateral transverse incision at the lateral edge of the right rectus as an aid in reaching the cæcum; this certainly endangers the tenth intercostal nerve.

ADVANTAGES COMMON TO TRANSVERSE INCISIONS

All modifications of the upper abdominal incision, transverse in all layers, present certain definite advantages over all forms of vertical incisions, including the so called Kammerer incision in which the rectus is retracted laterally out of its sheath. These have been discussed in such detail by the authors mentioned, especially Moschcowitz and Sloan, that to do more than enumerate the points of superiority would be superfluous: (1) Injury to the nerve supply is avoided. (2) The posterior aponeurosis of the flat muscles, the main supporting structure in the upper abdomen, is split parallel with the direction of its fibers. (3) Intra-abdominal exposure is greatly improved, necessitating far less packing, handling, and retraction of viscera. (4) Closure is always facilitated. (5) Postoperative course in the hospital is distinctly smoother with noticeably less tendency to vomit, little pain on respiration, and shorter confinement to bed with consequent economic gain. (6) There is suggestive evidence that the risk of respiratory complications is less. (7) Decreased risk of hernia and adhesions and better cosmetic result.

DISADVANTAGES OF VARIOUS TYPES OF TRANSVERSE INCISIONS

It has been said already that various modifications of the original transverse incision of the type of Maylard and Sprengel have been devised to correct minor difficulties as they occurred to the individual operator. It is not to be expected that any single incision will best meet all requirements of upper abdominal surgery in the experience of any individual but a critical discussion of the good and bad points of each, though these be in part

only theoretical, is desirable rather than otherwise.

1. (a) All the incisions that avoid cutting the rectus muscle (Bakes, Sloan, Singleton, Collins, Mason) involve the dissection of two large separate layers (skin and fat, rectus muscle) free from each other and from the underlying posterior aponeurosis, with the inevitable creation of extensive "dead space." Indeed, Singleton says, "A collection of lymph may occasionally show beneath the skin some 2 or 3 weeks later, but if left alone it will be absorbed within a few weeks." Our experience with fluid collections has been less happy, as they have usually become infected, requiring irrigation or through-and-through drainage. (b) In our experience, extensive retraction of the rectus in any direction causes hæmorrhage from the vessels posterior to it which is harder to locate and stop than if it were anticipated during cross division of the muscle; it occurs, moreover, at an unpredictable time during the operation. (c) When the rectus is retracted laterally, it is often sufficiently in the way during simple cholecystectomy seriously to limit one's room unless the linea alba be also divided. (d) Medial retraction of the rectus is apt to injure its nerve supply by stretching and (e) it blocks access to the linea alba when one wishes to divide it after once having started intra-abdominal procedures. (f) Bilateral exposure, that is, transverse division of the linea alba and posterior aponeurosis of both sides with dissection and retraction of both rectus muscles (Sloan), involves about twice as much cutting during opening and suture during closure as simple bilateral transverse division of all layers; this can readily be confirmed by measuring with a centimeter rule the total length of the incisions in different layers. (g) Incision of the same layer in two directions, with the production of "points," is considered undesirable in all surgical procedures. This is particularly true of fascial planes which are relatively avascular structures.

2. (a) Those incisions which are designed with divisions of different layers in different directions or at different levels, producing a "muscle lined" wound through which intra-abdominal tension does not have a direct path to the outside are open to the objections already cited in the cases of incisions of Sloan and Singleton. (b) The rectus flap operation of Perthes frees the rectus medially, divides it transversely at a low level, then turns it upward and laterally; the exposed posterior aponeurosis is incised close to, and parallel with, the rib margin. Collins' incision for the bile tracts is similar in its treatment of the posterior aponeurosis, the skin and anterior aponeurosis being incised diagonally from above and medially downward and laterally and the rectus muscle retracted laterally from its sheath. This location of the incision in the posterior aponeurosis is not strictly parallel with its fibers and involves some cross-division of them (Meyer); above all, it is in such a position that if a hernia should occur, repair would be next to impossible through lack of tissue in the superior shelf. We can find no reports on the incidence of hernia with these incisions, but the risk seems prohibitive to their use, which is not true of any of the objections cited to the other incisions discussed.

3. The classical incision, transverse in all layers and cross-dividing the rectus muscle has only one real objection, which is that the incision is carried straight down at one level through all planes and therefore offers a direct path to the outside through which intra-abdominal tension may be exerted. Evisceration as the result of extensive wound infection is noted by only one author (Meyer) and that in a case of presumed tetanus infection from catgut. However, incisions through different planes are more nearly ideal if staggered and we feel that we have evolved a muscle lined incision that meets this one theoretical objection. We can find no other evidence in the literature that transverse division of one or both recti is detrimental *per se* than the statement that there is some feeling against it.

PERSONAL EXPERIENCE AND SUMMARY OF CASES

Our own experience is limited to 28 cases during the past 16 months and we are now using routinely the incision to be described for all operations in the upper abdomen. The following is a summary of the essential circumstances of these cases.

1. The first 6 had a vertical incision carried down through skin, fat, and anterior aponeurosis, followed by retraction of the rectus muscle medially and transverse division of the posterior aponeurosis and peritoneum. In the next 13 cases, a classical transverse division of all layers was made in one plane. In the 9 remaining, the "staggered" incision was employed. The linea alba was incised 11 times; part or all of the rectus of the opposite side was incised 4 times.

2. The following intra-abdominal maneuvers were carried out: 17 cholecystectomies with incidental exploration of the common duct once; when present, the appendix was removed through the same incision except in 3 cases, in two of which supplementary McBurney incision was made at the same time; in the third instance it

was done on the eighteenth postoperative day. Two explorations of the common duct with choledochostomy through T-tube; 5 cholecystostomies with Pezzar catheter; 1 splenectomy; 1 anterior pylorectomy (Judd) and appendectomy; 1 ileosigmoidostomy; 1 exploration and closure (inoperable kidney tumor).

3. Of these patients, 11 weighed more than 170 pounds and of these only 3 were men.

4. Spinal anæsthetic was used in one case (splenectomy). Nitrous oxide plus novocain infiltration of the skin incision line and block at the outer border of the rectus was used in the others; supplementary ether was added in 2 cases, both of them simple cholecystectomies. All patients except the one operated on under spinal anæsthesia were given our routine pre-anæsthetic medication of 10 grains of phenobarbital sodium (in divided doses) and 3 grains of pento-barbital (Nembutal) orally with atropine but no morphine.

5. Five patients vomited one or more times in the first 24 hours after operation; 10 had to be catheterized during this period.

6. The average number of days in bed after operation was 9.3 and the average number of days in hospital after operation was 13, leaving out of account 5 patients. Of these, 2 were kept in bed 14 and 18 days, respectively, before subsequent perineorrhaphy and appendectomy; 2 were kept in bed 16 and 23 days, respectively, because of extensive wound infection requiring irrigation with Dakin's solution, and neither has developed a hernia after 5 and 9 months; the fifth patient was kept in bed 20 days to allow spontaneous healing of a previously made therapeutic fæcal fistula.

7. One pulmonary infarction occurred and another patient developed a streptococcus pneumonia and empyema subsequent to acute pyelonephritis. Both patients recovered.

8. Two hernias have appeared, both subsequent to complete transverse division of all layers:

Mrs. H. S., aged 41 years, height, 5 feet 3 inches; weight, 175 pounds. Following simple cholecystectomy she vomited once 48 hours after operation, had considerable bloody drainage from her incision on the fifth day after operation. The drain was removed on the ninth day. She was allowed up in a chair on the tenth day. She vomited again the following day. Appendectomy was performed on the eighteenth day, following which recovery was entirely uneventful except that bile drainage persisted until she was discharged from the hospital 28 days after cholecystectomy. One month after discharge a defect in the incised rectus could be felt, but a definite bulging could not be demonstrated until 4 months after operation.

Mrs. J. K., aged 39 years; height, 5 feet, 5 inches; weight, 205 pounds (cholecystectomy through vertical right rectus incision 7 years previously). She was nauseated after having taken 10 grains of sodium phenobarbital before going to operating room. After exploration of the common duct she vomited five times in first 24 hours and two to three times daily thereafter for 6 days; again on the ninth day. Penrose drain was removed on the ninth day. She was out of bed on the eleventh day, and was discharged on seventeenth day. Monthly examination did not reveal hernia until 4 months later.

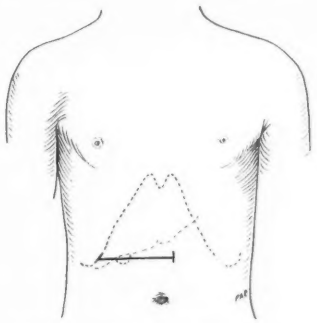


Fig. 2. A transverse skin scratch made across the liver border at the gall-bladder level; it connects a second scratch at the rib margin with a vertical third scratch 2 centimeters to left of midline.

We think that the continued bile drainage (source unknown) and a small hæmorrhage into the wound interfered with healing or led to too early absorption of sutures in the first case and that the continued vomiting in the second case was the important direct factor. We do not spare ourselves the reflection that better judgment would have been shown in postponing operation on the second patient, who obviously had an idiosyncrasy for phenobarbital sodium as shown by the onset of nausea after the second 5 grain dose. Her final dose (pentobarbital) was, of course, withheld. In neither case did gross infection of the wound occur. Both patients are now on weight reducing regimens and repair of the hernias should be far easier than in the case of vertical incisions.

TECHNIQUE OF INCISION

For the gall bladder and bile ducts, the skin incision should be marked with a preliminary scratch as shown in Figure 2. The operating table is tilted so that the patient's head is higher than his feet. The costal margin, then the liver edge, as determined by percussion, are marked. The line of incision is then marked transversely from a point just to the left of the midline to the liver margin and continues laterally to the rib margin. When the abdomen is opened through this transverse line, one will usually find the gall bladder just at this level and a little to the right of the middle of the incision.

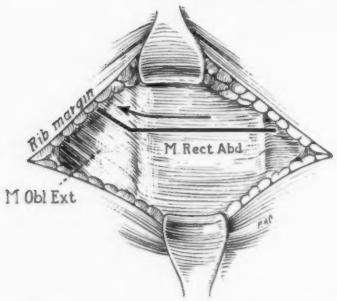


Fig. 3. Skin and fat have been retracted; the anterior rectus aponeurosis is split at the *highest* level between its fibers beginning at the midline and continuing diagonally upward across the rib margin.

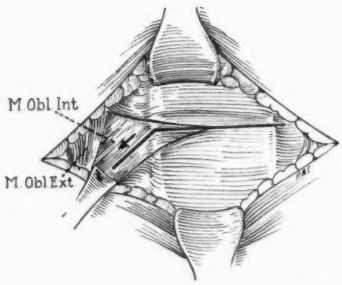


Fig. 4. The external oblique is retracted downward allowing the fibers of the internal oblique aponeurosis and muscle to be split in the direction of the arrow.

A definite routine should be followed in making the incision. After the skin and fat have been incised, the fat is brushed gently off the anterior fascial aponeurosis for a width of 2 centimeters. At the *upper* edge of this exposed area the anterior aponeurosis is opened from the midline to the lateral border of the rectus, and from this point the incision is continued laterally and upward between the fibers of the external oblique (Figure 3 shows more extensive dissection of fat from anterior aponeurosis for the sake of clarity). A narrow retractor is inserted into the lateral angle of the incision and pulls the lower border of the external oblique downward and laterally (Fig. 4), thus exposing the internal oblique and its fascia which are then split laterally from the edge of the rectus. At this point it will usually be found that the aponeurosis anterior to the rectus has retracted sufficiently to expose 2 centimeters of the muscle throughout its width; if it has not, the lower flap of anterior aponeurosis should be dissected off to that extent. A hæmostat is inserted under the rectus, lifting it gently, and the muscle is divided along the *lower* edge of the exposed area, starting at the lateral border (Fig. 5). With retractors in the lateral angle of the incision drawing the external oblique downward and the internal oblique upward the transversalis muscle, fascia, and peritoneum are incised (Fig. 6) at the *upper* level of exposure, which is in the same plane as the incision through the anterior aponeurosis. The incision is carried to the linea alba if opening of the common duct is not planned; when exploration of the ducts is to be done the linea alba is divided.

SUMMARY

The drawings do not bring out the treatment of the rectus muscle described, but this is shown in the diagram in Figure 6, in which it is seen that the anterior and posterior aponeurotic structures are incised at a higher level than the rectus muscle which, on closure, comes down like a tongue in a groove to a level 2 centimeters nearer the umbilicus, its line of division being covered anteriorly and posteriorly by intact fibrous structures rather than by suture lines. From the aspect of the suture lines in the fascial structures, this is a muscle-lined wound.

For most operations on the biliary tract we find that little extension of the fascial splits lateral to the outer border of the rectus is necessary. If more room is needed, particularly in operations on the ducts, the direction of the extension is always toward the midline and if further exposure for probing of the common duct is required the linea alba should be divided unhesitatingly. It has not yet been necessary to extend the incision for the purpose of routine inspection of the pylorus and duodenum during simple cholecystectomy. If still more exposure is needed after the linea alba is divided, the anterior and posterior aponeuroses of the opposite side may be incised and the rectus retracted or divided. We made a left sided incision for splenectomy in the case of a ruptured spleen and found it so large that division of almost the entire width of the right rectus muscle was necessary to its delivery. The patient, a 68 year old woman, has a perfect abdominal wall 11 months after operation. The incision, made on either side, can be extended laterally so that the kidney is readily accessible to a transperitoneal operation. In order to accomplish this without restriction it is advisable and almost necessary to divide either the internal or the external oblique muscle in a direction that cross cuts some of its fibers. This is theoretically

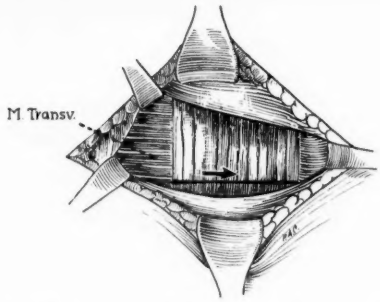


Fig. 5. The rectus muscle is exposed as far as possible by downward retraction of its coverings, then cross divided in the direction of the arrow at as *low* a level as possible.

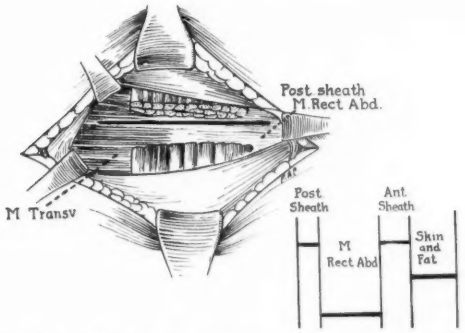


Fig. 6. The transversalis muscle and fascia are split between their fibers in a transverse direction at the same *high* level mentioned in connection with Figure 3 for the division of the anterior aponeurosis. (The diagram low right illustrates a staggered line of incision with muscle lined wound when closed.)

undesirable but is probably of little practical consequence since the other two of the three flat muscles are split, thus leaving an abdominal wall sufficiently strong for all practical purposes.

After operations on the biliary tract we bring drains out obliquely through the split in the flat muscles at the lateral border of the incision. The tendency of these muscles to pull together very quickly blocks any opening made in them and an oblique drainage tract through the abdominal wall is probably far better than one piercing it directly like the spoke of a wheel radiating from the hub. Intra-abdominal pressure exerted radially in all directions must tend to cause the collapse of an oblique tract by forcing the inner against the outer wall.

We wish to warn the surgeon using this incision that he will probably find himself spending more time working on the abdominal wall than within it until he has familiarized himself with the procedure; such was our experience. But opening the abdomen becomes as easy, in time, and quite as rapid by this method as through the Kammerer incision (paramedian incision, retracting the rectus laterally from its sheath); closure is as quickly done in all cases and is often incomparably simpler and more certain. Exposure is vastly better than through the upper angle of a vertical incision, the small intestine shows little tendency to push out over the lower shelf of the wound, one pack usually sufficing to protect adjacent viscera from the operative field. These advantages during operation bear heavy dividends in the postoperative course of the patient, both immediately and remotely.

NOTE.—Since this article was submitted for publication two experiences with transverse incision are of interest. On May 23, 1933, the large postoperative hernia on Mrs. J. K. was very easily repaired, fascia lata suture from the patient's thigh being used to resuture strong anterior and posterior aponeuroses which were readily identified. Weight reduction from 205 to 172 pounds was brought about before repair was attempted. Mrs. T. B. had abdominal exploration for compensated cirrhosis of the liver associated with chronic cholecystitis on May 2, 1933. She developed ascites subsequent to operation and had almost continuous hæmatemesis until the twelfth postoperative day when suddenly evisceration took place through the incision, the transverse colon and omentum being extruded onto the skin. Immediate secondary suture of the incision was done, under spinal anæsthesia. No traces of catgut were found but there had been obvious partial healing. Resuture was accomplished with ease, and the suture held until the patient's death from liver failure a week later.

BIBLIOGRAPHY

1. BAKES, J. Arch. f. klin. Chir., 1911, xcvi, 205.
2. COLLINS, C. Surg., Gynec. & Obst., 1908, vi, 413; Tr. West. Surg. Ass., 1908, p. 257.
3. FARR, R. J. Am. M. Ass., 1917, lxix, 1683.
4. JONES, D., and MCCLURE, W. Surg., Gynec. & Obst., 1930, li, 208.
5. KEHR, H. Arch. f. klin. Chir., 1912, xcvii, 74.
6. KOENIG, F. Zentralbl. f. Chir., 1912, xvi, 529.
7. MASON, J. T. Arch. Surg., 1929, xix, 129.
8. MAYLARD, A. Brit. M. J., 1907, ii, 895.
9. MCARTHUR, L. Surg., Gynec. & Obst., 1915, xx, 83.
10. MEYER, W. Ann. Surg., 1915, lxii, 573; J. Am. M. Ass., 1917, lxix, 1677.
11. MOORE, W. J. Ann. Surg., 1922, lxxv, 70.
12. MOSCHCOWITZ, A. Ann. Surg., 1916, lxiv, 268.
13. PERTHES. Zentralbl. f. Chir., 1912, ii, 1249.
14. QUAIN, E. Arch. Surg., 1920, i, 585.
15. SINGLETON, A. O. Southern M. J., 1931, xxiv, 200.
16. SLOAN, G. Surg., Gynec. & Obst., 1927, xlv, 678.
17. SOUTHAM, A. Brit. M. J., 1924, ii, 513.
18. SPALTEHOLZ. Handatlas der Anatomie des Menschen, 4th ed., ii, pp. 275–279.
19. SPRENGEL. Arch. f. klin. Chir., 1910, xcii, 536; Zentralbl. f. Chir., 1912, xxxix, 809.

DYSFUNCTIONAL UTERINE BLEEDING

Results in Treatment with Extracts of the Urine of Pregnant Women

GEORGE VAN S. SMITH, M.D., AND JOHN ROCK, M.D., BROOKLINE, MASSACHUSETTS
From the Free Hospital for Women and the Fearing Research Laboratory, Brookline

THE measures in common use for the treatment of dysfunctional uterine bleeding are usually rest, high calcium diet, injections of calcium or hæmostatic serum, administration of preparations of ergot or corpus luteum, curettage, exposure to X-rays or the local application of radium. Not infrequently the disturbance will cease spontaneously. Occasionally these medical measures tide the patient over. Successful results have been reported with corpus luteum, although the preparations available for clinical use show no merit experimentally. Often simple curettage is sufficient. More often it is necessary to resort to more drastic procedures with X-rays or radium because the other methods fail.

Dysfunctional uterine bleeding is thought to be due to the same factors that probably take part in the bleeding of menstruation, namely, some action of the anterior hypophysis on an endometrium that has been exposed to the secretion of the ripe ovarian follicle. Unlike menstruation, however, it is thought to be similar to the bleeding of monkeys, which frequently is not associated with ovulation, formation of a corpus luteum, and proliferative changes in the endometrium.

The amenorrhœa of pregnancy and possibly other amenorrhœas are associated with persistence of a corpus luteum. Conversely, the ovaries of patients with dysfunctional flowing commonly fail to contain a corpus luteum. Menstruation has frequently been observed to start early following the operative removal of an active corpus luteum. Experimentally, Smith and Engle have recently demonstrated in monkeys that a potent lipoidal extract of corpora lutea inhibited the flowing that otherwise would have occurred consequent to the administration of hypophyseal extract and estrin followed by castration. The logical treatment, then, of dysfunctional flowing would seem to be with corpus luteum, were a preparation suitable for human use available. Since extracts of corpus luteum cannot yet be employed clinically, attention was turned to extracts of the urine of pregnant women (prolan, antuitrin S, fol-lutein, luteinizing hormone) which characteristically produce corpora lutea when injected into immature mice and rats and normal rabbits. Because of their ability to luteinize the ovaries of experimental animals and because of their suitability for injection into humans, these extracts have been employed in the treatment of dysfunctional bleeding on the assumption that luteinization would take place and the flowing cease physiologically without recourse to the less rational methods mentioned. They have not been shown, however, to cause luteinization in humans in the amounts given and the actual mechanism of their therapeutic action still remains unsolved.

This report covers a total of 56 cases treated between January, 1931, and August, 1932, of which 24 had had menorrhagia of 2 months' to 10 years' duration and 36 had had metrorrhagia of 9 days' to 2½ years' duration. Although the distinction between menorrhagia and metrorrhagia can at best be only rough, this division of the cases seemed worthwhile for the purpose of this study. All the cases received intragluteal injections of antuitrin S (Parke, Davis & Co.). Until midsummer, 1931, the material was labelled "luteinizing hormone—50 rat units per c.cm." Since that time its potency has been labelled as 100 rat units per cubic centimeter. A rat unit is the smallest amount that will give discernible luteinization in the ovaries of immature rats by the Aschheim-Zondek technique. Due to the difficulties attending the extraction and purification of large quantities of this hormone and to deterioration, the consignments have often not tested as high as designated potency. This factor, combined with variable dosage, a necessary feature in testing a new substance clinically, has made it hard to evaluate results, and especially so in the type of disturbance herein concerned.

The chief obstacle to the administration of antuitrin S has been a reaction, of more or less severity, in the form of chills, headache, fainting, nausea, vomiting, and fever, which has occurred within 12 hours following injection. This has followed in 21 per cent of the 412 injections given. The patients have also complained a little of local soreness. It has been impossible to predict whether or when these reactions will take place. Some lots of antuitrin S have given more reactions than others. The earliest batches not only were more potent in the laboratory but also

seemed more efficacious clinically and caused no reactions.

Menorrhagia. Twenty-four patients complained of profuse and prolonged flowing at the time of menstruation. They were all between 17 and 42 years of age. Fourteen are considered cured in that their periods have been normal for 2 to 14 months following treatment. (Eleven have had normal periods for 5 to 14 months.) Eight of these had been ill for 2 months to 1 year; 4 had been troubled for 1 year (1 had pelvic inflammation); 1 had been handicapped 5 years and the last for 10 years. This last patient is 4 months pregnant, having had ten normal catamenias after treatment. Two years previously she had undergone operation for endometriosis. In 3 instances the menstruation after treatment started 5 days late. The dose of antuitrin S, both for these and the other cases in this report, varied from 2 to 9 injections of 2 to 10 cubic centimeters at a time over a period of 2 to 25 days. Most often the dose consisted of 4 to 6 injections of 5 to 10 cubic centimeters over 4 to 10 days.

Six patients of the menorrhagia group were temporarily benefited. The first (28 years old; symptoms for 2 years) stopped flowing during the first course of injections, but started again profusely 11 days later. The flowing ceased during a second course of injections and three normal catamenias have supervened. The second (37 years old; symptoms for 1 year) had 2 series of injections with a normal period after each. She later had a recurrence and was treated with X-rays. The third patient (32 years old; symptoms for 3 years following removal of a dermoid cyst of the right ovary, not relieved by curettage and resection of the left ovary for corpus luteum and retention cysts 2 months previously) had three normal menstruations after treatment, with a little intermenstrual staining. One series of injections stopped the bleeding of the fourth patient (17 years old; profuse periods for 3 years since menarche) and 3 normal periods followed. During the next 3 months her menstruation was frequent, irregular, and prolonged. The fifth (35 years old; profuse and prolonged catamenia for 6 months) had less flowing with one course of injections and then had two normal catamenias. A second course failed to control a recurrence. It has since been learned that she went to another clinic, where castration was performed. The sixth patient, a girl of 20 years, had had much abnormal flowing for 3 years, during which time she had been curetted twice, had received a small dose of radium twice and treatment with X-rays once. The first injections stopped her bleeding and she had three uneventful catamenias thereafter. A second time antuitrin S seemed to control excessive bleeding and again the next period was normal. She then missed a period. At present recurrent flowing has just ceased again with treatment.

The hormone failed to be of any obvious benefit to 4 patients with menorrhagia of 3 months', 5 months', 1 year's, and 5 years' duration, respectively. No explanation for these failures can be found. The patients were apparently no different in respect to severity of flowing or to diagnosis from the helped cases and there was no noteworthy variation in the treatment.

Metrorrhagia. Thirty-two patients complained of prolonged bleeding. They were between 14 and 47 years of age. Fourteen stopped flowing coincident with treatment and have had no further trouble for 1 to 14 months. (Nine have been well for 6 to 14 months.) They are briefly summarized as follows:

1. Miss T. 21. Flowing 24 days. Catamenia regular for 8 months after injections.
2. Mrs. O'K. 44. Flowing for 3 months. Three normal periods have followed injections.
3. Mrs. B. 31. Profuse and irregular flowing for 2 years, 6 months. One year before, curettage and resection of ovary for endometrioma. After treatment she menstruated regularly for 10 months.
4. Mrs. B. 31. Profuse flowing for 10 days. Treatment was followed by two normal periods.
5. Mrs. R. 23. Flowing 9 months. Fourteen normal catamenias have occurred since injections.
6. Mrs. M. 43. Bleeding for 1 month. Then well for 10 months.
7. Mrs. R. 25. Flowing 25 days. For 5 months after treatment there was no flowing at all. Then there was a normal period; the next was missed and again there was a normal period. She was 5 months pregnant at the last report.
8. Mrs. B. 45. Flowing for 20 days. Regular catamenias for 11 months after the course of injections.
9. Mrs. S. 25. Flowing for 2 months—ceased with treatment and had not recurred 1 month later.
10. Mrs. R. 39. Profuse and irregular bleeding for 1 year, 4 months. No relief from a curettage. Regular catamenias for 4 months since treatment.
11. Miss Z. 20. Flowing for 9 months. Had had a curettage without relief; then a curettage with removal of one ovary without benefit. She has now had 4 normal periods.
12. Mrs. A. 28. Flowing 21 days. After treatment her next two periods were very scant and 4 months of amenorrhœa have since followed.
13. Miss C. 28. Flowing for 6 months, not relieved by curettage on two occasions. She has now had normal catamenias for one year.
14. Miss H. 32. Flowing 3 months. She has been well for 14 months since treatment.

The optimum dosage in this group was 20 to 40 cubic centimeters of antuitrin S given in 3 to 10 cubic centimeter amounts over a period of from 3 to 10 days.

Sixteen patients were benefited to a greater or less degree. With all of these bleeding stopped during or soon after injections. Nine had no further trouble for 2 to 14 months. (Seven were well for 3 to 14 months.) These 9 histories are briefly reviewed:

1. Miss F. 19. Flowing for 4 months, unrelieved by a curettage. With one series of injections the bleeding stopped. Two normal catamenias supervened. The next period was missed. Then there was constant staining for a month, not inhibited, and possibly stimulated, by a course of small doses of antuitrin S. Following another normal period, flowing began and did not cease until 2 months after a third treatment. For 2 months amenorrhœa ensued. A fourth series of injections seemed to stop recurrent bleeding and there have since occurred two regular catamenias, each, however, of 2 weeks' duration.

2. Mrs. F. 26. Flowing 26 days. Relief, coincident with injections, persisted for 7 months. Then prolonged slight staining ceased during another treatment.

3. Mrs. G. 37. Flowing for 3 months—ended after injections and did not recur until 7 months later.

4. Mrs. D. 47. Flowing 1 month. Four months of amenorrhœa came after treatment and then very slight constant staining ensued.

5. Mrs. L. 30. Pulmonary tuberculosis. Flowing for 5 months, having had curettage and radium (50 milligrams for 8 hours) for the same complaint 7 months before. Normal periods occurred for 4 months after a series of injections. After that for 5 months her periods have come every 3 weeks and have lasted 5 days.

6. Mrs. G. 38. Duration of flowing was 6 months. Two months before injections curettage and multiple small myomectomy had been performed with only slight relief. She was well for 2 months after one series. Then staining ceased during a second series and three normal catamenias followed. During the next 9 months there was a little staining between periods.

7. Miss H. 14. Flowing for 6 months; ceased with injections and six normal menstruations occurred. Recurrent flowing ceased with further injections, but staining started 10 days later. This disappeared after three 10 cubic centimeter injections of antuitrin S.

8. Miss P. 14. Bleeding for 20 days. After one course of injections 3 months of amenorrhœa ensued and then 2 months with only a catamenial stain. Recurrent flowing of 5 weeks' duration became, if anything, more profuse with injections (these again were small amounts). A third series of injections was given; the bleeding stopped and there has been no trouble for 1 month.

9. Miss P. 28. Flowing for 2 years, which stopped for the first time during treatment. Then a normal period occurred during treatment. The next three catamenias were of 14, 8, and 26 days' duration, respectively. With another series the bleeding increased before ceasing. Three months of comparative relief followed, but then the trouble recurred as badly as ever and the patient had curettage and radium.

Of the 7 remaining patients in this "benefited" group, one has failed to report since her relief with treatment. The second (35 years old; flowing for 4 months unrelieved by curettage and conservative operation for pelvic inflammation) had a recurrence of bleeding 2 weeks after injections and has not reported since.

3. Mrs. M. 24. Flowing, of 7 months' duration, ceased with injections and a normal period occurred. Seven profuse periods have since followed a second series.

4. Mrs. C. 40. Nine days of profuse bleeding, which stopped with treatment but recurred 2 weeks later. At operation pelvic inflammation was found.

5. Mrs. B. 40. Flowing for 7 weeks. Bleeding decreased but did not stop with injections. At operation, performed within a week of treatment, pelvic inflammation was found. The ovaries showed no gross or microscopic change which could be attributed to antuitrin S, although four 10 cubic centimeter doses had been given (4000 rat units, according to designated potency).

6. Miss McL. 30. Flowing for 6 weeks. Stopped with treatment and recurred 5 days later; then ceased within 3 days. The patient has now been well for one month.

7. Mrs. S. 25. Flowing for 5 months. Relieved by injections. A month later curettage and myomectomy were done at another hospital. Flowing recurred after operation and had lasted 4 months when the patient returned. Again it stopped coincident with injections. At the last report, 6 months later, the patient stated that she had had a hysterectomy.

There were two complete failures. One of these patients had had radium (100 milligrams for 6 hours) a year before hormone treatment, which did not affect her recurrent flowing. The other continued to stain despite injections. Both ultimately had radium.

DEDUCTIONS

It is almost certain that some of the patients in this series would have improved without treatment. More of the others almost certainly would have come to operative procedures and irradiation. Cessation of flowing or normal menstruation followed treatment sufficiently often to be more than coincidental.

Antuitrin S has seemed to be more effective when administered while patients were flowing, e.g., in controlling rather than preventing menorrhagia. In a few instances, especially when small doses were given, it has seemed to cause a temporary increase in bleeding or a prolonged staining. On the other hand, amenorrhœa and delayed menses occurred often enough in relation to treatment to seem caused by it.

The fact that it was of value in 2 cases of endometriosis, 4 cases of pelvic inflammation, and 2 of fibroids may be taken as evidence that bleeding in these conditions may be primarily dysfunctional and associated only indirectly with the diseases.

The employment of this hormone in bleeding cases presupposes as careful a diagnosis as possible, the most important feature of which is to rule out malignant pelvic disease.

LABORATORY DATA

In performing Aschheim-Zondek tests on urines from patients with dysfunctional flowing, we have

found that they often contain a hormone which produces follicle-ripening in the ovaries of immature rats (the so called prolan A effect or anterior pituitary reaction I). Fluhmann has described this effect, using bloods of "women with irregular profuse periods at the time of the menopause, and in younger patients with too profuse and too frequent menses." From 15 of the patients of the group herein reported morning urines were injected into immature rats in 6 cubic centimeter amounts. In all, 31 specimens were tested. Eighteen were from patients who were flowing at the time of collection and 14 of these gave positive prolan A effects. Of the 4 negative urines, 3 were collected after treatment had been started, although the flowing had not ceased. From patients who were not flowing when the urine was collected, on the other hand, 11 out of 13 specimens were completely negative. These results suggest that the hypophyseal-like hormone found in the urines in these cases may be connected with the etiology of the condition. Further, the findings intimate that antuitrin S may possibly have its beneficial effect through direct inhibition of this prolan-A-like hormone, for in the case of 5 patients who were flowing and whose urines gave positive tests at the start of treatment, a disappearance of this substance from the urine was coincident with the cessation of symptoms after the course of injections. This finding has recently been duplicated in 12 more cases. As a control, tests were performed with urines from one woman who received no antuitrin S but whose flowing was temporarily stopped by curettage. They were positive for prolan A both before and after operation.

Novak and Hurd have already expressed the opinion that antuitrin S may have a direct effect on a "bleeding factor" possibly of hypophyseal origin. Our early results support their opinion in that administration of antuitrin S was associated with the disappearance of a hypophyseal-like hormone from the urine. Preliminary experiments in which the hypophyses of spayed rats that had received antuitrin S were transplanted into immature females, have indicated a direct effect of this extract upon the anterior hypophysis. If it could be definitely shown that dysfunctional flowing is the result of abnormal hypophyseal activity and that antuitrin S directly inhibits or changes the abnormal factor, there would be a logical basis for explaining the mechanism of the beneficial effect of this hormone without the necessity of considering the corpus luteum at all.

SUMMARY

The rationale for the employment of extracts of the urine of pregnant women in the treatment of uterine bleeding of dysfunctional origin has been presented. Antuitrin S, an extract of the urine of pregnant women, was administered to 56 patients with dysfunctional uterine bleeding with the following gross results: cured 28; benefited 22; unrelieved 6. The cessation of bleeding accompanied treatment so often and in many cases so rapidly as to leave little doubt of the specificity of the hormone, especially considering the variable potency of the preparations supplied. A limited number of laboratory findings have suggested a clue concerning the mechanism of this hormone's therapeutic action, namely, the possibility of a direct action on a hypophyseal hormone.

REFERENCES

1. Fluhmann, C. F. J. Am. M. Ass., 1929, xciii, 672.
2. Idem. Am. J. Obst. & Gynec., 1930, xx, 1.
3. Novak, E., and Hurd, G. B. Am. J. Obst. & Gynec., 1931, xxii, 501.
4. Smith, P. E., and Engle, E. T. Proc. Soc. Exper. Biol. & Med., 1932, xxix, 1225.

We are indebted to Dr. O. Watkins Smith for co-operation in the planning and execution of the laboratory procedures, to Miss Alice Lyons for her constant help in the clinic and to Mrs. R. C. Crocker for much secretarial assistance

TUMORS OF THE PAROTID REGION

Studies of One Hundred and Thirty-Five Cases

JOSEPH McFARLAND, M.D., Sc.D., Philadelphia
McManes Laboratory of Pathology, University of Pennsylvania

THIS contribution is partly a continuation and partly an amplification of a paper entitled "Ninety Tumors of the Parotid Region, in All of Which the Postoperative History was Traced," that made its appearance in the *American Journal of the Medical Sciences*, December, 1926.[1] It is a continuation in that it tells what has happened to as many of those 90 cases as could be followed-up during the 5 years that have since elapsed, and an amplification in that 45 additional cases have been studied and introduced, in one way or another as what was known about them was found to be useful.

In each contribution I have made use of the expression "tumors of the parotid region" because experience early showed that few, if any, of the tumors are actually *of the parotid gland;* most of them being *in, upon, or adjacent to it.* This is certainly true of the typical "mixed tumors," some of which are scarcely "adjacent" in the strict sense,—as in Singer's case, in which the tumor was in the external auditory meatus,—and doubtfully true of certain apparently carcinomatous tumors of the region, that leave one in doubt as to whether they began in the gland and invaded the adjacent tissues and skin, or in the skin and adjacent tissues and invaded the gland. Among the specimens called "carcinoma of the parotid" in hospital laboratories and surgical records, both have repeatedly been met.

In the earlier contribution the whole subject—probable origin, nature, location, structure, appropriate treatment, and subsequent behavior—of these interesting tumors was covered, but always with particular stress upon the predominating group of "mixed tumors."

My personal observation and experience were supplemented by a review of the cases published in the literature, making total of 359. To them are now to be added 45 additional cases bringing the grand total of cases upon which the present contribution is based up to 404.

From the data formerly assembled it was concluded that the mixed tumors are peculiar, highly variable neoplasms, that they are not always easy correctly to identify or classify and that they behave in a manner so erratic as to make correct prognosis extremely difficult if not impossible Additional data and experience have not modified those conclusions.

Surgeon friends who read the paper asked my opinion and advice about matters upon which I could not venture with confidence. It, therefore, seemed expedient to collect more cases, add to the data, and attempt new methods of analyzing and utilizing the information thus gained.

A persistent endeavor was made to follow-up the old cases for another 5 years, and to secure and follow-up additional cases in which operation had been done 5 years or more ago. A few cases in which operation was but recently done have been used for the size and age data. Case numbers up to and including 90 belong to those reported in the earlier contribution.

It has been more easy to find and study sections of the tumors than to obtain the case histories. Sometimes no clinical notes were available, sometimes they were fragmentary; in less than half of the cases were they at all complete. Some cases with limited data could only be used in certain tabulations, because some particular datum was useful and had to be omitted from others because it was lacking.

It must, therefore, be remembered that the cases mentioned in one relation, are not necessarily the same cases mentioned in others.

With one or two exceptions, all of the patients had been operated upon, and specimens had been sent to the laboratory of a hospital for microscopic examination. My discovery of the tumors took place in the laboratories where I was permitted to study the microscopic slides, after which through the laboratory record, the case history, and the kindness of the surgeon, I finally traced the patient and learned the subsequent course of events.

The follow-up many times failed, usually because of the death or removal of the patients to other cities. Of the many follow-up letters received from patients, not one expressed anything but appreciation of the fact that someone was interested in their progress, and some of the patients appeared to have been anticipating with pleasure the receipt of the semi-annual letter of inquiry.

[1] clxxii, 804.

On page 22 of the original paper, there is a tabulation of 44 cases of typical "non-recurrent mixed tumors," and it will not be without interest to learn what has happened to them during an additional period of 5 years. Eight of the 44 patients —Cases 3, 8, 10, 11, 15, 37, 40, and 42—had already died of causes other than the tumor at the time the paper was published. In the years that have elapsed, 7 more patients have died: Case 2, patient free from recurrence 9 years, death from nephritis; Case 4, patient free from recurrence 11 years, death from pulmonary tuberculosis; Case 5, patient free from recurrence 16 years, death from cardiac failure, age 78 years; Case 9, patient free from recurrence 18 years, death from carcinoma of urinary bladder; Case 28, patient free from recurrence 16 years, death from apoplexy; Case 31, patient free from recurrence 7 years, death from pneumonia; Case 43, patient free from recurrence 3 years, cause of death not known, but death was not from the tumor.

During the same period 10 patients were, for various reasons, lost to the follow-up but it is known that in Case 13, patient enjoyed freedom from recurrence for 9 years; in Case 17, for 2 years; in Case 21, for 11 years; in Case 22, for 1 year; in Case 24, for 5 years; in Case 26, for 9 years; in Case 33, for 4 years; in Case 35, for 2 years; in Case 38, for 7 years; in Case 44, for 4 years.

There has been only one known case of recurrence, Case 16. The patient is now (1932) living and the small tumor is being treated with X-rays. In his last letter he reported "doing well."

Of the original 44 cases, 18 patients are known to be living and well at the time of this writing; they were operated upon at periods varying from 5 to 21 years ago: Case 36, patient free from recurrence for 5 years; Case 32, for 7 years; Case 30, for 8 years; Case 41, for 8 years; Case 23, for 9 years; Case 34, for 9 years; Case 20, for 10 years; Case 25, for 10 years; Case 18, for 11 years; Case 19, for 12 years; Case 14, for 13 years; Case 39, for 13 years; Case 7, for 16 years; Case 27, for 17 years; Case 29, for 17 years; Case 1, for 19 years; Case 12, for 19 years; Case 6, for 21 years. In addition there are some new cases: Case 99, free from recurrence for 5 years; Case 97, for 5 years; Case 95, for 6 years; Case 94, for 7 years; Case 105, for 15 years; Case 106, for 16 years; Case 91, for 17 years; and Case 103 for 24 years.

TABLE I.—FOLLOW-UP IN FORTY CASES

Years of freedom from tumor	Living and well, case Nos.	Dead, case Nos.	Lost to the follow-up, case Nos.	Totals
5	36, 37, 39	3, 8	24	6
6	95	0	0	1
7	32, 94	11, 31	38	5
8	30, 41	0	0	2
9	23, 34	2	13, 26	6
10	20, 25	0	0	2
11	0	4	21	2
12	19	0	0	1
13	14, 39	0	0	2
14	0	0	0	0
15	105	0	0	1
16	7, 106	5, 28	0	4
17	27, 29, 91	0	0	3
18	0	9	0	1
19	1, 12	0	0	2
20	0	0	0	0
21	6	0	0	1
22	0	0	0	0
23	0	0	0	0
24	103	0	0	1
				40 cases

TABLE II.—SMALL TUMORS—SMALLER THAN A WALNUT

No.	Pre-operative duration, years	Postoperative freedom, years	Recurrence	Died	Living and well	Lost	Size of tumor	Remarks
75	1¼	8	0	0	+	0	Bean	Microscopically suggested carcinoma
46	2	9	+	0	+	0	Hazel-nut	
33	10	4	0			+	Grape	
63	2	8	0			+	Marble	
52	4	7	+		+		Almond	
62	15	20	0	+			Hickory-nut	Died of acute indigestion, suddenly
104	5	13	?	+			Chestnut	Died of supposedly independent osteosarcoma of jaw

TABLE III.—TUMORS OF ORDINARY SIZE—WALNUT TO LEMON SIZE, INCLUSIVE OF BOTH

No.	Pre-operative duration	Postoperative freedom, years	Recurrence	Died	Living and well	Lost	Size of tumor	Remarks
97	5 mos.	5	o	o	+	o	Nut	
50	?	30	+++	+	o	o	Nut	Did not die of the tumor
1	8 yrs.	17	o	o	+	o	Walnut	
7	10 yrs.	16	o	o	+	o	Walnut	
8	6 yrs.	5	o	+	o	o	Walnut	Died of pulmonary tuberculosis
11	8 yrs.	7	o	+	o	o	Walnut	Died of heart disease
12	4 yrs.	18	o	o	+	o	Walnut	
23	16 yrs.	9	o	o	+	o	Walnut	
24	20 yrs.	5	o	o	o	+	Walnut	
26	4(?) yrs.	9	o	o	o	+	Walnut	
27	8 yrs.	17	o	o	+	o	Walnut	
30	5 yrs.	8	o	o	+	o	Walnut	
34	32 yrs.	9	o	o	+	o	Walnut	This tumor required 32 years to grow to peasize, then in 2 years grew to walnut size
35	6 yrs.	?	?	?	?	+	Walnut	
43	25 yrs.	?	?	+	o	o	Walnut	Cause of death not known
47	30 yrs.	16	+	+	o	o	Walnut	Died of pneumonia at 82 years of age
49	25 yrs.	11	+++	o	+	o	Walnut	
58	6 yrs.	12	o	+	o	o	Walnut	Died of kidney disease
68	3 yrs.	5	?	?	?	+	Walnut	
69	6 yrs.	10	o	o	+	o	Oyster	
81	1 mo.	o	+	+	o	o	Walnut	Unimproved by operation, had recurrence, died of tumor which may have been cancer
97	5 mos.	5	o	o	+	o	Walnut	
111	25 yrs.	?	?	?	?	+	Walnut	
112	3 yrs.	?	?	?	?	+	Walnut	
18	3 mos.	4	o	+	o	o	Plum	Died of acute appendicitis
39	7 yrs.	13	o	o	+	o	Plum	
40	18 mos.	?	o	+	o	o	Plum	Died immediately after 1st operation
44	1 yr.	4	o	?	?	+	Plum	
48	20 yrs.	6	+	o	+	o	Plum	
64	24 yrs.	9	o	o	o	+	Plum	
65	16 yrs.	16	o	o	o	+	Plum	
66	8 yrs.	3	o	o	o	+	Plum	
2	8 yrs.	9	o	+	o	o	Egg	Died of kidney disease
10	7 yrs.	?	?	+	o	o	Egg	Died of arteriosclerosis in 3 months
15	3 yrs.	3	o	+	o	o	Egg	Cause of death unknown—not the tumor
32	7 yrs.	7	o	o	+	o	Egg	
45	20 yrs.	13	+	o	o	+	Egg	
53	6 yrs.	?	++	o	o	+	Egg	
73	2 yrs.	9	o	+	o	o	Egg	Died of pulmonary tuberculosis
74	1 yr.	15	o	o	+	o	Egg	
76	2 yrs.	8	+	o	+	o	Egg	

TABLE III.—TUMORS OF ORDINARY SIZE—WALNUT TO LEMON SIZE, INCLUSIVE OF BOTH—Continued

No.	Pre-operative duration	Postoperative freedom, years	Recurrence	Died	Living and well	Lost	Size of tumor	Remarks
77	4 mos.	—	++++	+	o	o	Egg	Died of the tumor, perhaps cancer
110	6 yrs.	?	?	?	?	+	Egg	
93	4-5 yrs.	?	o	+	o	o	Thumb	Accidentally killed
39	7 yrs.	14	o	o	+	o	Seckel pear	
13	20 yrs.	9	o	o	o	+	Lemon	
22	10 yrs.	1	?	?	?	+	Lemon	
31	20 yrs.	7	o	+	o	o	Lemon	Died of pneumonia
67	6 mos.	13	o	o	+	o	Lemon	
80	1 yr.	—	+	+	o	o	Lemon	Died in a year of the tumor, perhaps cancer
87	8 mos.	11	+	+	o	o	Lemon	Died of the tumor

TABLE IV—LARGE TUMORS—THOSE OF SIZES LARGER THAN A LEMON

No.	Pre-operative duration	Post-operative freedom, years	Recurrence	Died	Living and well	Lost	Size of tumor	Remarks
9	20	18	o	+	o	o	Apple	Died of carcinoma of the urinary bladder
14	25	13	o	o	+	o	Goose egg	
71	many	2	o	+	o	o	Goose egg	Death unrelated to the tumor
20	10–15	10	o	o	+	o	Orange	
42	32	3	o	+	o	o	Orange	Died of diabetes; no recurrence
70	2	5½	o	o	o	+	Orange	
88	15	—	+	+	o	o	Orange	Died of the tumor in 2 years
36	7	5	o	o	+	o	Grapefruit	
37	10	—	—	—	—	—	Grapefruit	Died without treatment
38	18	11	o	+	o	o	Grapefruit	Death unrelated to the tumor
95	29	7	o	o	+	o	Grapefruit	
55	20	—	+	+	o	o	Two fists	Died of the tumor
109	50	—	o	+	o	o	Human head	Died at the operation

Table I shows 40 cases, old and new, living, dead, and lost, in which the patients are known to have enjoyed freedom from the tumor for 5 years or longer after operation.

GROWTH OF THE TUMORS

At this point it becomes desirable to place before the reader certain facts regarding the growth rate of mixed tumors that form the basis of certain important conclusions, and to that end beg the reader to refer to Tables II, III, and IV. In all but 2 or 3 cases, in which metric measurements of length, breadth and thickness were mentioned, the tumors have been described in the protocols as the "size of a walnut," etc. When all of the standards of comparison were listed no less than 16 sizes, beginning with a "pea" and ending with a "human head" were found to have been employed. It was impossible to take notice of all of these minute divisions, so the tumors have been divided into three principal divisions: (I) small tumors (smaller than a walnut); (II) ordinary sized tumors (from a walnut to a lemon, inclusive); (III) large tumors (larger than a lemon).

If this tabulation (Tables II, III, IV) be examined, the tumors will be found to have *a fairly regular average growth rate.* That is to say, the small tumors had an average pre-operative duration of about 5 years, the ordinary sized tumors, of about 10 years, and the large tumors of about

TABLE V.—COMPARISON OF SIZE AND DURATION

Size	Tumors	Average duration, years
1. Smaller than walnut	7	5
2. Walnut	23	10
3. Plum	8	9
4. Egg	14	6
5. Lemon	6	8
6. Apple, goose egg, and orange	7	18
7. Grapefruit or larger	6	20

TABLE VI.—REVISED COMPARISON OF SIZE AND DURATION

Size	Tumors	Average duration, years
1. Smaller than walnut	7	5
2. Walnut	20	12
3. Plum	5	15
4. Egg	7	7
5. Lemon	3	17
6. Apple, goose egg, orange	7	18
7. Grapefruit or larger	6	20

20 years. If we divide the tumors into a greater number of sizes, the occasional variations in growth rapidity accidentally intensified in some particular group result in a slight disorder, yet the average is pretty well maintained (Table V).

Perhaps the discrepancies in Table V depend upon certain of the tumors differing in kind from the others, the chief differences being very short pre-operative duration (a year or less), recurrence, and death of the patient. If such cases be eliminated, the results concerned with mixed tumors alone, show growth to be progressive and regular except for the group of egg size.

TREATMENT

The time-honored treatment of tumors of the parotid region is surgical excision, and is still generally practiced, though irradiation is being tried in an increasing number of cases, and in many circles seems to be meeting with a cordial reception in spite of the fact that the structure of the tumor really suggests a very unpromising field for success.

The value of any treatment can be estimated only by the results obtained, and the statistics published are in complete accord in finding that the excision of these tumors fails in from 25 to 30 per cent of the cases. But notwithstanding this high percentage of failures, and, perhaps on account of them, the method is not only continued, but patients are urged to undergo the operation at the earliest possible moment, first, because sooner or later it will be inevitable; second, because a small tumor is supposed to be more easily and certainly eradicated than a large one; and third, because if neglected the tumor may change from a benign to a malignant course. It may be well to consider to what extent these opinions are justified.

I. *What will happen to the patient if no treatment be instituted?* If a typical mixed tumor, as identified by its years of duration, its location, its circumscription, and its histological structure, gradual growth through many subsequent years is a fairly safe prognosis. There is no hurry, and relief from the deformity is the chief incentive to do something.

II. *What will happen as the result of treatment? Irradiation.* What we know may be of little value because not enough treated patients have been observed long enough to permit satisfactory comparison with the older and more widely practiced method of surgical excision.

Case 34. The tumor was operatively removed and X-ray treatments subsequently applied. At the end of 10 years there had been no recurrence, but that is what commonly happens without such treatments.

Case 46. The tumor, operatively removed, recurred in 9 years and 6 months. It was given X-ray treatments, and for 7 years has remained unchanged in size. That also sometimes happens, so it does not prove that the irradiation was useful.

Case 16. The tumor, operatively removed, recurred after 6 years, was again removed in 1930, after which radium treatments were given. There has been no return in two years, which is too short a time to mean anything.

Case 85. After three operative removals in 1905, 1915, and 1923, seven X-ray treatments were given without effect: the tumor continued to grow and finally caused death.

Case 88. After surgical removal in 1909 and 1924 and repeated X-ray treatments, the patient not having improved, died of the tumor.

Case 20. After surgical removal of the tumor in 1915 and 1922, the patient was given intensive X-ray treatments. There has been no return of the tumor (1932). Other tumors, twice removed, have also failed to return for periods of 10 years, where no X-ray treatments were given.

From this amount of evidence it is difficult to conclude that any benefit to the patients accrued from the irradiation.

Surgical excision. It is, of course, impossible for the pathologist to know about the conversations that go on between the patient with a tumor and the surgeon whose advice is sought, but the usual result is an operation at which the tumor is removed. Presumably the patient desires to be rid of an increasing physical deformity, and the surgeon to free him of such future trouble as the presence of the tumor may entail. After this radical treatment, some 70 per cent of the patients with tumors are never seen again. But 30 per cent of the tumors recur.

On page 24 of the earlier paper, there were tabulated 19 cases of mixed tumors that had recurred at that time, and it may be of interest to know what has since happened to them.

In the 3 cases—50, 54, and 58—death occurred from causes other than the tumors before the publication of the paper.

In the 3 cases—death occurred since publication of the paper from causes other than the tumor—in Case 56 from abdominal carcinosis not connected with the parotid tumor, and 5 years after its removal and with no recurrence; Case 62, from "acute indigestion," without any new recurrence in 20 years; Case 47, from "cardiac failure" at 78 years of age, and after 16 years of complete freedom from the tumor.

Three cases are known to be living and without recurrences at present: Case 48; Case 49, patient has had 15 years of freedom since the third operation; Case 61, patient has had 10 years of freedom since the second operation.

One case—46—the tumor was first removed in 1914; there was a recurrence in 1924, and although energetically treated with X-rays, the "lump remains."

Two cases—55 and 59—patients have died of the tumors after repeated recurrences.

Seven cases—45, 51, 52, 53, 57, 60, and 63—have been lost to the follow-up.

The urgency of the operation. Should any patients be advised to undergo immediate operation? Before this question can be answered it is necessary to recall that there are certainly considerable differences among the tumors, the most notable being in the length of pre-operative duration; those known to have existed for *years* usually showing a microscopic structure typical of "mixed tumors," those the duration of which is expressed in *months* an atypical structure more or less closely resembling carcinoma.

a. *Slowly growing tumors.* Let it be supposed that the tumor is small, has been recognized by the patient for 3 or 4 years. As has been shown in the tabulation given, such a tumor usually continues to grow slowly, doubling its size every 5 years or so. There need, therefore, ordinarily, be no hurry in removing it in so far as its growth is concerned. On the contrary, there may be excellent reasons for not disturbing it.

One of the most distressing accidents that may result from the operation is the destruction of the facial nerve that lies in close juxtaposition to many of the tumors. Two cases among personal acquaintances illustrate this complication.

Miss C. —, a charming spinster good to look at and delightful to converse with, discovered a "lump" behind the angle of the jaw. It was no larger than an almond, and could only be felt, not seen. Alarmed at the thought that it was a tumor, she sought advice, and learning that the operation for the removal would be perfectly easy and simple, permitted its performance. She recovered from the anæsthetic to find the whole right side of the face hopelessly paralyzed, and ectropion soon occurred. Subsequent "lifting of the face" was twice tried with little improvement, and for 5 or more years she has been distressed at what she sees in her mirror, and her friends at her changed and unsightly appearance. Had the operation been deferred, a swelling might now be apparent where the tumor was situated, but her face would retain its vivacious and cheerful expression, and she would have enjoyed years of happiness instead of mental anguish.

Mr. J. M.—Case 47—had a small "cyst" removed from the parotid region; it recurred almost at once but grew so slowly that at the end of 30 years it was only of walnut size. It caused what he considered to be an unsightly swelling, and after consultation it was operatively removed. He lived 16 years with facial palsy and ectropion, before he died suddenly, aged 78 years.

Six of the patients of this series (45, 48, 56, 103, 47, and 83) are known to have suffered in this way, only one case, 83, having made a good recovery. A "lump" upon the face would be vastly preferable to the distress of facial palsy with ectropion.

A second accident, salivary fistula, is rare, and only one of the patients, Case 2, complained about it, and about an operation for its cure having failed.

Is it not important to operate when the tumor is small because of the greater ease of operation and the complete removal of the tumor more certain? In this case it would seem as though the chief criterion of success must be the prevention of recurrence.

Among the tumors of this series concerning which the data are available, recurrences occurred in 30 per cent, fatality in 13 per cent; among the clinically and microscopically "mixed tumors," the recurrences were 25 per cent and the fatalities only 3 per cent.

Curiously enough recurrences are more frequent when the tumor is removed while small. In the tabulation showing the tumors arranged according to size, it will be found that in Group I, tumors smaller than a walnut, there are 7, of which 2 recurred, 28.5 per cent; in Group II, tumors of ordinary size, there are 51, of which 11 recurred, 21.5 per cent; and in Group III, large tumors, there are 13, of which 2 recurred, 16.1 per cent. Thus it seems that the smaller the tumors are, the more apt they are to recur.

If it be objected that this makes no allowance for the probable differences in the nature of the tumors, it must be remembered that it is impossible accurately to determine the nature of the tumor before operation, if it can be done at any time.

But assuming that a short pre-operative duration and an ambiguous microscopic appearance characterize tumors to be regarded as malignant, and eliminating them, the ratio will stand thus: Group I, small tumors, 7 with 2 recurrences, 28.5

TABLE VII.—RELATION OF GROWTH TO MALIGNANCY—OPERATION IN ALL CASES

Case	Size	Duration, mos.	Microscopy	Outcome
97	Nut	5	Mixed tumor	Living and well 5 yrs.
81	Walnut	1	Carcinoma (?)	Recurrence, continued growth, killed
18	Plum	3	Mixed tumor	No recurrence in 4 yrs., died of appendicitis
44	Plum	12	Mixed tumor	No recurrence in 4 yrs., lost
74	Egg	12	Carcinoma (?)	No recurrence, 15 yrs., living and well
77	Egg	4	Carcinoma (?)	Four recurrences caused death
67	Lemon	6	Sarcoma (?)	No recurrence in 13 yrs., living and well
80	Lemon	12	Carcinoma (?)	Died of carcinoma within a year
87	Lemon	8	Carcinoma (?)	Said to have lived 11 yrs. before dying of tumor

per cent; Group II, average tumors, 44 with 7 recurrences, 15.88 per cent; Group III, large tumors, 13 with 2 recurrences, 16.1 per cent, so that the same holds true—the highest percentage of recurrence results from operations upon the smaller tumors.

b. *Rapidly growing tumors.* Let it be supposed that the tumor, small or of ordinary size, has appeared and grown to its present dimensions in a year or less, should it not then be promptly removed? It is such tumors that give the greatest anxiety to surgeons, who always suspect them of malignant disposition. What is the evidence that rapidity of growth is indicative of malignant tendency? Table VII may give some information on the subject. It contains all of the tumors of rapid growth, and so all those the surgeon would certainly have recommended for immediate operation. In how far would he have been correct?

Here are 9 cases in all of which the growth was alleged to be of less than a year in duration and hence under suspicion of malignancy. Of these, 5 behaved as benign tumors, although 3 had a histological structure apparently inconsistent with such a prognosis. It is most interesting to see that the growths in Cases 97, 18, 44, 74, and 67, that should ordinarily have taken 10 years to reach the sizes at which they came to operation, grew to those sizes in an average period of 7½ months, without any evidence of malignancy. Therefore, as less than half of these rapidly growing tumors proved to be malignant, rapidity of growth is an insecure guide to follow.

c. *Are patients with apparently malignant growths benefited by operation?* In solving this problem the great difficulty lies in reaching a conclusion as to what is meant by the term malignancy as it is applied to these tumors. The microscope, ordinarily the authority on this subject, fails. Thus:

Case 67. The growth appeared to be microscopically a lymphosarcoma, but the patient was alive, well, and without recurrence 11 years after one operation.

Case 69. The growth also appeared to be a lymphosarcoma, but the patient was alive, well, and without recurrence 10 years after one operation.

Case 72. The growth, when examined microscopically, appeared "carcinomatous," but the patient lived 16 years, with no recurrence after one operation, to die of cirrhosis of the liver.

Case 73. The growth appeared "carcinomatous," but the patient lived 9 years, with no recurrence after one operation, to die of tuberculosis of the lungs.

Case 74. The growth appeared "carcinomatous," but the patient lived 15 years, with no recurrence after one operation, and was then lost.

Case 75. The growth appeared "carcinomatous," but the patient lived 8 years, with no recurrence after one operation, and was well in 1932.

Case 76. The growth appeared to be carcinoma, but the patient lived 8 years, with no further recurrence, after a second operation and is living and well in 1932.

Case 83. The growth appeared to be carcinoma, but the patient lived 15 years, with no further recurrence, after a second operation and is living and well in 1932.

Seven cases of apparently malignant tumors cured by one or two operations is a high rate of cures and it may be that the surgeons are to be congratulated upon their success, but suspicion must rest upon the results because of the uncertainty of the microscopic diagnosis.

In 13 other cases, microscopically resembling carcinomata, the patients have all died of their tumors, under conditions and in a period consistent with that diagnosis. This gives a total of 21 cases of seemingly malignant tumors, of which 40 per cent did not, and 60 per cent did, behave as such.

From an examination of the fatal cases, one cannot escape the conviction that the benefits of operation seem to be very small (Table VIII), as in most of the cases the tumor progressed promptly to its fatal termination.

But this subject must not be concluded without mention of 2 cases in which the surgeons take

TABLE VIII.—RESULTS IN THIRTEEN CASES MICROSCOPICALLY RESEMBLING CARCINOMA

Case	Size	Duration	Treatment	Result
81	Walnut	1 mo.	Excision	Died of tumor in a little less than 3 yrs.
40	Plum	18 mos.	Excision	Died immediately after operation
77	Egg	4 mos.	Excision	Recurred 3 times; 3 later operations, died in 3 yrs. 1 month.
80	Lemon	12 mos.	Excision	Died of the tumor in a year—general carcinomatosis
87	Lemon	8 mos.	Excision	Died of the tumor in 2 yrs.
55	Two fists	20 yrs.	Excision	Died of the tumor in 8 yrs.
88	Orange	15 yrs.	Excision and X-rays	Died of the tumor in 2 yrs.
78	?	6 mos.	Excision	Died of the tumor in 7 yrs.
79	?	15 mos.	Excision	Died of the tumor within yr.
82	?	12 mos.	Excision	Never improved, died of the tumor
84	?	2 yrs.	Excision	Died of the tumor in a few months
86	?	2 yrs.	Excision 1924 and 1926	Died of the tumor in 1926 or 1927
89	?	?	Excision 1909	Died of the tumor in less than 2 yrs.

great pride, and to which they point as triumphs of surgery:

Case 76. The tumor in 2 years grew to the size of an egg and was operated upon in 1920 and again, for recurrence, in 1924. The tissue removed had a histological appearance so similar to carcinoma that it was unhesitatingly so classified. The patient, however, is living and well (1932), 8 years later.

Case 83. A walnut-sized tumor was removed in 1917, followed by operations for the removal of recurrences in 1919, 1920, and 1923. The tumor was similarly, unhesitatingly classified as a carcinoma, but the patient was living and well, and working as a truck-driver in 1932, 9 years later.

Do these cases indicate malignant tumors cured, will they return later, or was the microscopic appearance deceptive and the tumors after all of low grade malignancy? Perhaps future observation will tell.

Is operation really a useful procedure? If, as has been shown, operation is not urgent because the tumors usually have a regular and slow rate of growth; if it is more difficult successfully to eradicate them when small than when large; if there is always danger of damaging the facial nerve and so occasioning greater deformity and misery than the tumor itself entails; if rapid growth is no index of malignancy; if the microscopic appearance of the excised tissue offers no guarantee of exemption from recurrence, and in many cases is uncertain as to malignancy and prognosis; and if the benefit conferred by excision in the cases that turn out to be malignant is very slight, why should the surgical excision of these tumors be practiced? Only because it is generally supposed that the 70 per cent of cases in which no subsequent symptoms are manifested, are *cured*. But here, again, arises a great uncertainty. Who is cured and when? For example, in Case 48 there was a recurrence after 6 years of freedom from the tumor; in Case 52, after 7 years of freedom; in Case 46, after 9 years of freedom; in Case 49 there were three recurrences after 11 years of freedom; in Case 45, there was a recurrence after 13 years of freedom; in Case 47, after 16 years of freedom; in Case 50, after 30 years of freedom.

If any one of these patients had died during the period of freedom, it would have been supposed that the disease was *cured*. But not so, it recurred. The discovery of the long interval of freedom after which recurrence might occur was the chief reason for continuing to study the tumor in preparation for the present contribution.

If the tabulation on one of the earlier pages, showing 19 cases carefully followed, and known to be living and well at the present time be examined, it will be noted that not one of them has outlived the possible period of recurrence as indicated.

Recurrence is the horrible menace of the parotid tumors. There is no certainty of exemption from recurrence, and once it happens, the chances seem to be that it will be repeated again and again. There are several theories to explain recurrence:

1. In addition to the tumor that the surgeon sees and carefully removes, there may be other and smaller ones that he does not see (multicentric growth) and that later develop to noticeable size. Under these circumstances the recurrence can be regarded as an entirely different tumor, and may not make its appearance for a long time as shown in Table IX.

TABLE IX.—RECURRENCES

Case	First operation	Second operation	Third operation	Free intervals in years	Termination
46	1914	1924		10	Living with the recurrence in 1932
62	1895	1910		15	Died without further recurrence in 1930, 20 yrs.
45	1895	1910		15	Died without recurrence in 1923, 13 yrs.
58	1910	1912		2	Died without recurrence in 1924, 12 yrs.
47	1886	1916		30	Died without recurrence in 1932, 16 yrs.
56	1911	1923		12	Died without recurrence in 1929, 6 yrs.
61	1915	1922		7	Has been well for 8 yrs., no recurrences
48	1913	1925		12	Has been well for 7 yrs., no recurrences
49	1904	1911	1915	3, 4	Has lived 7 yrs., no recurrences
50	1861	1892	1911	31, 11	Died 19 yrs. after the third operation, no recurrence
98	1914	1919	1927	5, 8	Living 1932, 5 yrs. without recurrence

It seems unlikely that recurrences at such wide intervals can be other than new tumors arising in the same manner as the primary tumor did.

2. For any of several reasons the surgeon may not be able to effect a complete eradication of the tumor, and, knowingly or unknowingly, leaves fragments that continue to grow and perhaps to invade. The following cases may be explained in this way:

Case 59. First operation 1925, second (9 months later) 1925, third 1929—died of the tumor in 1932.

Case 51. First operation 1910, second 1912, third 1918, fourth 1924, fifth 1929—has since lived 2 years without recurrence.

3. If the capsule of the tumor be opened during the operation, tumor cells may be transplanted and produce recurrence. This theory is supported by the successful cultivation of "mixed tumor" tissue *in vitro*. Prompt, unencapsulated and infiltrative types of growth might be expected under these circumstances, and it may be that some of the carcinoma-like tumors thus arise. If the following ambiguous tumors were members of the mixed tumor class, the implantation of their cells at the time of operation may account for what subsequently happened:

Case 77. This tumor recurred 4 times in 6 months and terminated fatally.

Case 81. The operation for removal failed, the tumor continued to grow and was fatal.

Case 82. The patient never improved after the operation and died of the tumor.

Case 53. After operation the tumor began to grow again, at once. (This was one of the hard cartilaginous varieties of "mixed tumor.")

The escape of the tumor tissue from its capsule through incision for biopsy examination or at surgical excision appears to modify the type of growth in some cases by permitting infiltration of the surrounding tissues. Such a change seemed to have taken place in Case 59. The patient had a tumor of 5 years' duration which was removed in 1925, and proved, upon microscopic examination to be a mixed tumor. It was described by the pathologist to the hospital as a "fibro-chondrosarcoma of the parotid." In 9 months there was a recurrence that was removed in 1926. In 1928, I examined this patient and found a second recurrence of hen's egg size, most of the surface of which was well defined, though at one or two points it seemed vaguely to infiltrate the surrounding tissues that were swollen and firm, like carcinoma. Another excision was performed, and though parts of the surface were found to be covered with a capsule, the uncovered portions infiltrated the adjacent tissues. With the excised tumor there came to the laboratory a rounded body supposed to be an invaded lymph node. It was, however, a separate small tumor mass with nothing to suggest that it had ever been a lymph node. The patient died, in 1931, of the tumor, which had not given metastasis so far as could be determined. Unfortunately, the description of what happened is vague—"The tumor grew quite large, invaded the orbit so that the eye protruded, and she died when it went to her brain."

Do mixed tumors become malignant in the sense of transforming into sarcomata or carcinomata? In the former paper this question was considered at considerable length. The tumors supposed to have become sarcomatous did not behave as sarcomata usually do, or those supposed to have become carcinomatous as carcinomata usually do, the difference in behavior being the extreme rarity of metastases.

It is very difficult to overcome the prevalent disposition to classify all malignant tumors as

members of one or the other of the time-honored groups—carcinoma or sarcoma. There are certainly malignant tumors, non-metastatic (gliomata) and metastatic (melanomata) that cannot be so classified, but are a law unto themselves, and perhaps these "mixed tumors" belong in a category of their own.

When it is considered that no one who has had one of these tumors can ever be regarded as exempt from the danger of recurrence; that a tumor that had occasioned no other disturbance than that caused by its physical bulk (size of an olive) for as long as 30 years (Case 50), when excised, was followed by a recurrence that grew rapidly to the size of an orange; that in Case 88, a tumor that had grown for 15 years to reach the size of an orange, and in Case 55 one that had required 20 years to reach the size of two fists, when operatively meddled with assumed so violent a course of recurrence, increase in volume, compression and obstruction of adjacent passages, ulceration, and necrosis as to prove fatal in 2 years or so; that these tumors, if injured, are apt to undergo necrosis, ulceration, hæmorrhage, and infection from which there is no recovery, and that in the great majority of cases the ill effects are entirely limited to the region in which they grow, it seems not only reasonable to consider them malignant, but as characterized by a peculiar and individual type of malignancy quite different from that of more commonplace growths.

Mixed tumors of the parotid do not, therefore, *become* malignant, rather they *are* malignant, though this is true in varying degrees in different cases.

If this view be adopted it will be easy to understand Kornblith's case of a mixed tumor of the submaxillary gland, excised and twice recurrent, that was followed 3 years later by the appearance of metastatic mixed tumors of histological structure exactly like the primary tumor in the lungs and many other organs. This tumor certainly did not become malignant, it was so. Neither did it undergo sarcomatous or carcinomatous "degeneration,"—it was and remained a "mixed tumor" of the cylindromatous type. The same is true of the only case of metastasis that has come under my observation (Case 115), that of a parotid region tumor with an enlarged lymph node in the neck. Microscopic examination of the lymph node showed *a nodule of mixed tumor*—not of carcinoma.

Does the age at which the tumors first appear have any bearing on their subsequent behavior? The available data upon this subject are shown in the following outline:

I. *Non-recurrent mixed tumors:*
40 cases average 34.5 years of age at first appearance of the tumor—
Minimum age—16 years
Maximum age—67 years

II. *Recurrent mixed tumors:*
10 cases average 30 years of age at first appearance of the tumor—
Minimum age—14 years
Maximum age—44 years

III. *Repeatedly recurrent mixed tumors:*
5 cases average 21.9 years of age at the first appearance of the tumor—
Minimum age— 3 years
Maximum age—50 years

IV. *Fatal cases of all kinds:*
11 cases average 52 years of age at the first appearance of the tumor—
Minimum age—26 years
Maximum age—75 years

At first this tabulation appears to be quite intriguing: in the first three groups it seems that the earlier the tumor appears, the more trouble it is likely to give. But the figures may be of no importance as the extremes in each group show great divergence, and Group IV with the greatest age of primary appearance and which, therefore, should be the least distressing, is made up of repeatedly recurrent fatal tumors. But the number of tumors upon which the computation is based is not only too small to give accurate information, but the variability of the tumors themselves probably makes the computation valueless. For example: if, because a patient's age is 42, it were supposed that his tumor would probably prove malignant and fatal, the probability would be completely offset by the fact that in Group I in 12 of 40 cases the patients are above 40 years old. If, on the other hand, the patient being only 22 it were inferred that the tumor would probably recur again and again, it would be made equally improbable because in the same Group I in 6 out of 40 cases the patients are less than 22 years of age.

Is there any means by which a prognosis can be reached? If it be admitted that all mixed tumors are potentially malignant as has been suggested, it is not with reference to their benignancy or malignancy that the prognosis is desired, but with reference to the *probable degree of the malignancy* in each particular case. This matter was considered 5 years ago, and the conclusion reached that if the tumor has reached a size bringing the patient to operation in a year or less, and if the tissue removed appears "carcinomatous," the prognosis is ominous.

CONCLUSIONS

1. Tumors of the parotid region, unlike most other tumors, vary greatly in histological structure and clinical manifestation, without any constant correspondence of the two by which accurate diagnoses and prognoses can be arrived at.

2. Tumors of the microscopic structure supposed to be typical of "mixed tumor" frequently cause death after repeated recurrence, and infiltrative growth, but very rarely with metastasis to distant organs.

3. Tumors of microscopic structure indistinguishable from sarcoma or carcinoma, after simple excision, appear to be cured, in that the patients remain in good health for many years.

4. After excision of any type of parotid tumor, recurrence may take place at any time up to 30 years.

5. This makes it difficult to be certain that any case is cured.

6. It also makes it certain that the tumors are malignant in themselves, and not by virtue of any sarcomatous or carcinomatous "degeneration."

7. Except in the rarest cases there is no metastasis, so that the type of malignancy is peculiar.

8. The "mixed tumors" have a fairly regular rate of growth that is ordinarily very slow.

9. Occasional tumors of rapid growth are not necessarily more dangerous than others.

10. When growth is so rapid as to bring the patient to operation within a year, and the excised tissue resembles carcinoma, the prognosis is bad.

11. The age at which the tumor appears has no bearing upon benignancy or malignancy.

12. It is not advisable to operate upon the tumors when small, as the smaller tumors are the more apt to recur.

13. Such data as are here offered suggest that except to improve the appearance and ease the patient's mind, it might be just as well not to operate upon these tumors.

14. It seems, as usual, that very little benefit to the patients has accrued from operations directed toward the removal of the rapidly malignant tumors.

15. Irradiation has not yet been shown to be of any benefit.

16. Whatever is to be decided upon, haste is probably never necessary, and when operation is contemplated, the accidents of facial palsy, salivary fistula and recurrence should be carefully considered for fear that more harm than good be done.

THE SURGICAL TREATMENT OF RECTAL TUBERCULOSIS

W. A. FANSLER, M.D., F.A.C.S., MINNEAPOLIS, MINNESOTA
Assistant Professor of Surgery, University of Minnesota; Consulting Proctologist, Glen Lake Sanatorium
C. K. PETTER, M.D.
Senior Resident Physician, Glen Lake Sanatorium

IN 1924, the Department of Proctology of Glen Lake Sanatorium for Tuberculosis was created. The average register of some 700 patients has offered an interesting field of observation during the past 8 years. The paucity of accurate records and laboratory data on rectal tuberculosis and the variation of opinion as to its frequency and method of treatment was startlingly apparent upon investigation of medical literature available at that time. I at once determined to outline a definite plan for systematically studying cases at Glen Lake. In 1926, Doctor Petter became associated with the staff in a full time capacity, and since that time has been my co-worker in this enterprise. His lasting enthusiasm and tireless energy has made this work possible. This present paper is the fifth presented on the subject since 1925, and it is interesting to observe that the conclusions recorded after 8 years of study, vary considerably from those recorded in 1925. It is likely there may be some change in our present ideas, but we do feel that these 8 years have enabled us to determine some facts which are of permanent value.

For the purpose of determining whether or not a lesion is tuberculous, we use the three following methods: (1) the inoculation of a guinea pig with pus from the lesion, (2) the inoculation of a guinea pig with tissue from the lesion, and (3) the microscopic examination of tissue removed from the lesion.

In the first two we must always consider the possibility of contamination with the tubercle bacilli from more distant foci, hence, we consider the last named method the most valuable, and the only one not subject to the possibility of error. In 85 per cent of our cases the diagnosis was made from microscopic sections of tissue, and in only 4 per cent were inoculation methods positive, where tissue examinations were negative. The criterion acceptable on proving the lesion tuberculous, is the presence, microscopically of actual tubercle formation. More recently we have felt in certain very early cases that a microscopic picture termed "tuberculoid" might possibly be included as conclusive evidence. In this case there is an infiltration of lymphocytes and epitheloid cells, which have not grouped themselves in true tubercle formation, but are scattered throughout the section. The epitheloid cells are diamond or club shaped, and occur singly or in groups, and are often surrounded by lymphoid cells. Special stains occasionally show tubercle bacilli around epitheloid cells.

Surgery is indicated in rectal tuberculosis for two reasons: first, to relieve the local condition which is often painful, and second, and often more important, to lessen the load of tuberculosis and infection which the patient is carrying. As an emergency measure, such as drainage of an abscess, surgery may be indicated almost regardless of the patient's general condition. As a rule, however, surgery should not be attempted unless the patient is in fair condition and there is reasonable certainty of the wound healing. The probability of the operative wound healing can be determined quite accurately in advance by the amount of fibrosis present in the lesion. Fibrosis is nature's method of healing tuberculosis, and if it is present to considerable degree in the rectal lesion, one may be quite sure that the patient is caring for his tuberculosis elsewhere, and that any operative wound will likewise heal promptly. This "fibrosis index" is most valuable in determining the advisability of surgical interference and the prognosis in a given case.

The following outline shows the chief types of rectal tuberculosis and the advisability of operating, or not operating:

1. *Perianal cutaneous tuberculosis.* This group may be divided into 4 classes: (a) tuberculous anal ulcer—varying amount of fibrosis present, usually operable; (b) tuberculosis cutis orificialis —terminal cases, fibrosis usually not present, not operable; (c) miliary tuberculosis of the anal skin—terminal cases, fibrosis usually not present, not operable; and (d) lupoid cutaneous tuberculosis—fibrosis present, always operable.

Perianal cutaneous tuberculosis is rare, there being only 18 cases in our series as compared with 152 cases of abscess and fistula. Of these 18 cases, 15 had tuberculous anal ulcers. In the primary stage, it cannot be definitely determined whether or not anal ulcers originate in the skin. In a typical case, the patient complains of definite pain, and perhaps some bleeding on defæcation.

TABLE I.—RÉSUMÉ OF PERIRECTAL ABSCESS AND FISTULA IN ANO

Total cases	152
Records inadequate, thrown out	19
In residence	29
Awaiting surgery	6
Terminal cases	23
Patients operated upon	104
Percentage of males	72
Percentage of females	28

Age range, 18 to 72 years; average 32 years

TABLE IA.—SUMMARY OF 104 OPERATIVE CASES

Other tuberculosis	Cases	Sputum positive	Laboratory positive	Healed	Dead
Far advanced pulmonary	80	77	72	72	8
Moderately advanced pulmonary	14	11	12	14	0
Minimum pulmonary	5	2	4	5	0
Bone	2	0	2	2	0
No clinical tuberculosis	3	0	3	3	0
Total	104	90	93	96	8
Percentage		87	89.4	92.3	7.7

	Per cent
Active tuberculosis present in	95
Active bone tuberculosis present	2
No demonstrable clinical tuberculosis present	3
Sputum positive	87
Proved tuberculous by (1) exudate in guinea pig or (2) tissue in guinea pig, or (3) tissue section or combination of (1, 2, 3)	89.4
Proved positive by tissue section alone	85
Laboratory work negative or none done	10.6
Healed	92.3
Patients died of other tuberculous lesions	7.7
Healed after re-operation	5.0
Patients discharged since 1926, total 1560	
Percentage with abscess or fistula in ano	3.0
Patients discharged, 1926 to 1929, total 1807	
Percentage with abscess or fistula	5.8
Patients now in residence with abscess or fistula.	6.0

Examination reveals a simple anal fissure. If untreated, the patient may continue to complain, and upon a second examination a week or two later, there is found a ragged, indurated, fiery red ulcer at the site of the previous simple fissure. Further examination usually reveals the sputum of the patient to be decidedly positive for tuberculosis, indicating the presence of an active lesion. If untreated, these ulcers become in appearance more like the chronic type of ulcer. At this stage we may be uncertain as to whether the lesion originated in the skin or whether the original infection was in the rectal mucosa of a crypt of Morgagni. Instead of penetrating to the deep structures and forming an abscess and fistula, the infection extends superficially and involves only the anal skin in the ulcerative lesion. The lesion usually occurs in patients with slight or only moderate resistance to tuberculosis.

Tuberculosis cutis orificialis occurs in the mucous membrane and skin adjacent to the anus in patients having no resistance to tuberculosis. It appears as an ulcer progressively invasive in character, destroying skin and sometimes mucosa, but not the deeper structures. No fibrosis is present and the condition occurs as a terminal complication. There were 2 cases in our series.

Miliary tuberculosis of the anal skin occurs in conjunction with highly virulent and rapidly fatal generalized miliary tuberculosis. This condition was not encountered in our series of cases.

Lupoid cutaneous tuberculosis occurs as a subcutaneous nodule covered by a bluish unbroken skin. As the condition progresses the skin becomes thin and shining and central necrosis and ulcer formation may occur. Lupoid tuberculosis occurs in patients with a well developed resistance to tuberculosis. There was 1 case in our series.

2. *Perirectal abscess and fistula.* In this second group are found by far the most frequent tuberculous lesions about the rectum. Perirectal abscesses vary greatly, depending upon the type of infection and the resistance of the patient. In one extreme we have a patient noticing the gradual formation of a painless, or nearly painless nodule, near the anus. This nodule may continue to enlarge for 2 or 8 weeks. Finally it becomes somewhat reddened over a small area, and a little later a small amount of thin flocculent seropurulent discharge is noted. Elevation in temperature, if present, is slight and is often not increased over that already present as a result of tuberculosis elsewhere in the body. This is a picture of a tuberculous abscess forming in a patient with good resistance to tuberculosis. In the other extreme, we have a patient who complains of severe pain, the rapid formation (24 to 48 hours) of an intensely red and tender mass near the anus. The temperature may be up to 103 or 104 degrees. If not incised, the abscess ruptures in a few days. This is the picture of a perirectal abscess occurring in a patient of low resistance, and it is not unlikely that the abscess is complicated by the presence of other organisms as well as the tubercle bacillus. All gradations between these two extremes occur. After the abscess has been drained and the acute symptoms have subsided, the fistula remains. The fistulas may be divided into four characteristic

clinical groups. Their appearance is dependent upon the patient's resistance and the virulence of the organism.

The first type presents a small external opening, which may or may not be, surrounded by a nub of scar tissue. If a probe be passed into the fistula, the tract will be found to be small in diameter and well surrounded by scar. This type has no clinical appearance to differentiate it from a simple pyogenic fistula. It occurs in persons with marked resistance to tuberculosis, or is due to an organism of low virulence.

The second type is characterized by a somewhat larger opening. Instead of scar, the margin of the skin about the opening appears to be thinned out and of a bluish-red appearance. There may be a little seropurulent discharge. When the probe is passed into the opening a cavity of some size is found. This usually lies rather superficially underneath the skin and the probe can be moved freely from side to side. If the opening is large enough, so that the interior of the cavity may be seen, it will be found to be lined with pale flabby granulations. The amount of scar tissue present is much less. This patient has a fair amount of resistance to tuberculosis.

The third type shows a definite eaten out cavity with an internal opening as large as the rest of the tract. It would seem that the infection is advancing and destroying everything before it. No fibrosis or other tendency toward healing is present. This type of case is seen in persons with a rapidly progressive case of tuberculosis, who have no resistance.

The fourth condition included under this head is the internal fistula or rectal ulcer. This condition occurs from a tuberculous infection in the rectal wall which produces an abscess between the mucosa and muscular wall of the rectum and does not appear externally. When seen after the abscess has broken down, there is found an opening in the rectal mucosa of varying size and a submucous cavity which also varies in extent. The variation of this picture usually corresponds in intensity with the first two types of fistulas just described.

3. Generalized tuberculous ulceration of the rectum corresponds with the third type of the fistulas just described. This condition is almost always associated with generalized tuberculous enteritis and is a rapidly progressing fatal condition.

When it is decided that surgery is indicated, it is important that it be done thoroughly. Failure to cure rectal tuberculosis is more often due to timidity rather than boldness. In a few words, it is necessary that all tuberculous tissue be destroyed and that all sinuses and overhanging edges of tissue be removed. A wide open wound, all parts of which are easily seen and which drains readily by gravity, should be left. After this it is usually only a question of careful dressing until the wound heals. The choice of anæsthetic is important. For obvious reasons general anæsthesia is usually not to be desired. We now do almost all of our work under spinal anæsthesia, 35 milligrams of procaine crystals being dissolved in 1 cubic centimeter of spinal fluid. This is ample for ordinary rectal operations.

TABLE II.—RÉSUMÉ OF PERI-ANAL TUBERCULOSIS*

Type	Cases	Treatment	Result
(3) Miliary tuberculosis	0		
(4) Lupoid tuberculosis	1	Cautery excision	Healed
(2) Tuberculosis cutis ani (orificialis)	2	1 general 1 cauterized twice	Died Died
(1) Tuberculous anal ulcer	15	10 cauterized 5 no treatment	Healed Terminal cases—Died

*All patients had far advanced tuberculosis; all showed positive sputum.

Our actual operative methods have undergone some changes. In the beginning we used what was the generally accepted method, namely: sharp dissection with a scalpel and scissors. In the cases with marked fibrosis, the results were very good. In the border line cases with little fibrosis, we found that frequently there was reinfection with tuberculosis, and even with secondary operations, numerous cauterizations, and caustic applications to secure healing, good results were not secured in all cases. We then began to remove the lesions with the actual cautery, or if some delicate dissection was required, to use sharp dissection followed by cauterization of the wound with cherry red heat. Our results improved immediately, but we felt that there was still room for improvement. The cautery is a rather clumsy instrument for doing some of the work in the rectum, and there is an eschar which is slow in separating after the operation. Also there is considerable postoperative pain. About a year ago we began using the endotherm knife and at present believe that it is an improvement over anything else used. It can be used in all cases, even for the most careful dissection, and we feel that the time of postoperative healing has been definitely reduced. Likewise, postoperative pain is slight, many patients requiring no opiates after operation.

Our method is simple, consisting of removing all diseased tissue with the cutting current, and then coagulating all parts of the wound with the coagulating current. Patients operated upon in this way show the same resistance to re-infection as those operated upon with the cautery, but there is not the extensive eschar. This in turn is reflected in a shorter healing time.

Postoperative care is simple but extremely important and must be done carefully and faithfully. Hot sitz baths once or twice daily for all but bed patients is routine. The wound is dressed once or twice daily. Mercurochrome or iodoform gauze is gently packed into the wound to stimulate and keep it healthy. Granulations are kept down with silver nitrate stick. The medication may be varied as indicated, but the most important consideration is that the wound be frequently dressed and kept stimulated with gauze. Under these methods our results have been most gratifying. The statistical charts give a definite idea of the results secured.

TREATMENT OF FRACTURES OF OUTER END OF CLAVICLE

AARON H. TRYNIN, M.D., BROOKLYN
From the Service of Dr. S. Kleinberg, Israel Zion Hospital, Brooklyn

IN a recent publication I called attention to the use of the Boehler clavicular splint in the treatment of dislocation of the acromioclavicular joint. It was pointed out that a condition for which open operation has always been resorted to in order to obtain a good functional, cosmetic, and anatomical result can now be treated conservatively without discomfort to the patient. Fractures of the outer end of the clavicle with upward displacement of the inner fragment present the same problem. Although reposition of the fragments may not be difficult, the maintenance of reduction has never been accomplished satisfactorily. Open operation here too has been the usual method of treatment. In this paper I wish to present a case of this type of fracture and the results obtained with the use of this splint.

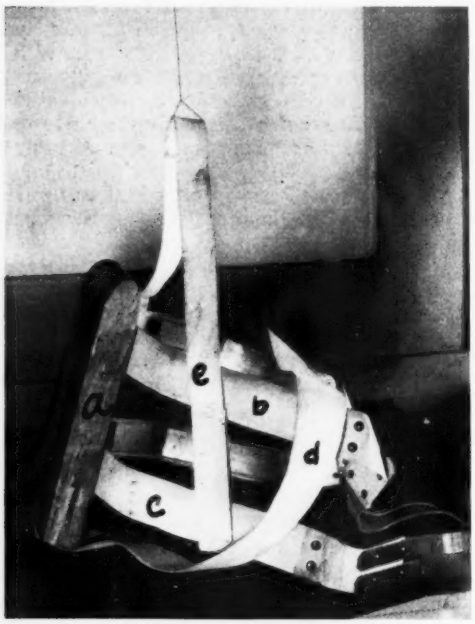


Fig. 1. The Boehler clavicular splint.

The apparatus, as pointed out (Fig. 1) consists of a board, *a*, 30 centimeters long, 15 centimeters wide and 5 centimeters thick. The part fitting into the axilla is smoothed into a Gothic arch to fit the concavity of the axilla. Two malleable iron ribbons, *b* and *c*, 50 by 4.4 centimeters, with two short belts made of webbing are fastened to the main part of the splint and are used to fasten the splint to the trunk. A third webbing, *d*, attached to the bottom of the splint is fastened over the normal shoulder and is used to raise the injured shoulder. A fourth belt, *e* with a buckle is introduced under the lower iron ribbon and is used to press the inner fragment of the clavicle down. All parts are well padded and under the webbing used to exert pressure on the clavicle a felt pad is placed.

The purpose of the treatment is to counteract the reflex contraction of the trapezius which draws the inner fragment of the clavicle upward and to overcome the weight of the arm which draws the outer fragment down. These forces act similarly in acromioclavicular dislocation. Desault and Velpeaux bandages have been used but after removal the deformity has been found to have re-

Fig. 2. Fracture of the outer end of the clavicle with separation of the fragments.

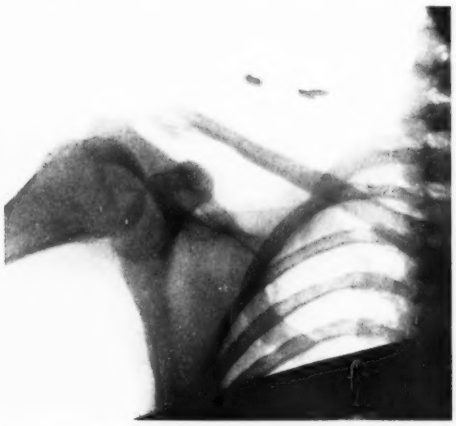


Fig. 3. Reduction obtained after application of the splint.

curred. Shaar has described an elastic traction splint for acromioclavicular separation. Traction on the clavicle downward is supplied by rubber tubing and a canvas strip which is attached to a canvas strip support to the arm. This is similar to the method advocated by Currie, consisting of two buckled webbing straps over the acromioclavicular joint and around the flexed forearm. No provision is made for elevating the acromion or acromial end of the clavicle while the inner fragment is pulled downward. The extremity is immobilized to the side throughout the period of treatment and in older individuals causes a stiffness of the shoulder and elbow joints. The downward pull on the clavicle in both methods depend on the weight of the arm and once the arm is raised or the forearm is flexed, this downward pull is lost and the fragments are displaced.

In treating this type of injury, three important requirements must be satisfied. Constant downward traction must be maintained on the inner fragment, constant upward pressure must be exerted on the outer fragment and there should be freedom of motion of the shoulder and elbow joints. The advantage to the patient is quite evident. Prolonged immobilization causes atrophy of the muscles which often taxes the patience of the surgeon to overcome. The clavicular splint described satisfies all these requirements.

CASE REPORT

M. N., age 16 years, sustained a fracture of the right clavicle on May 16, 1932. A visible prominence was present at the region of the acromioclavicular joint. Roentgenogram (Fig. 2) showed a fracture of the outer end of the clavicle with upward displacement of the inner fragment. Simple pressure on the clavicle reduced the fracture

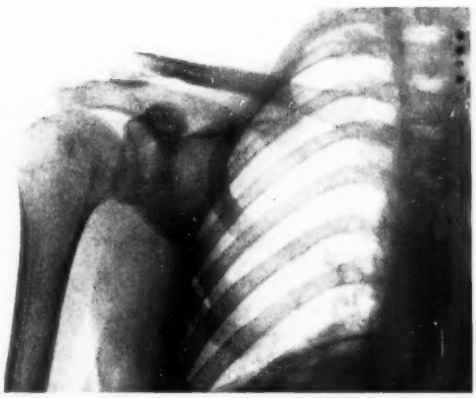


Fig. 4. Eight weeks after the fracture, 2 weeks after removal of splint.

but this reduction could not be maintained with the ordinary retaining bandages. The clavicular splint was applied. Roentgenogram after 24 hours (Fig. 3) showed the fracture reduced. The apparatus was maintained for 6 weeks. A final roentgenogram taken 8 weeks after the injury—2 weeks after removal of splint—showed the fragments in good alinement and early callus formation.

REFERENCES

1. Currie, D. I. An apparatus for dislocation of the acromial end of the clavicle. Brit. M. J., 1924, i, 570.
2. Shaar, C. M. Upward dislocation of the acromial end of clavicle. J. Am. M. Ass., 1925, xcii, 2083.
3. Trynin, A. H. Conservative treatment of incomplete dislocation of the acromioclavicular joint. J. Bone & Joint Surg., 1932, xiv, 421.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

FRANKLIN H. MARTIN, M.D.....Managing Editor
ALLEN B. KANAVEL, M.D.....Associate Editor
LOYAL DAVIS, M.D.....Associate Editor

DONALD C. BALFOUR, M.D.....Associate, Editorial Staff

JULY, 1933

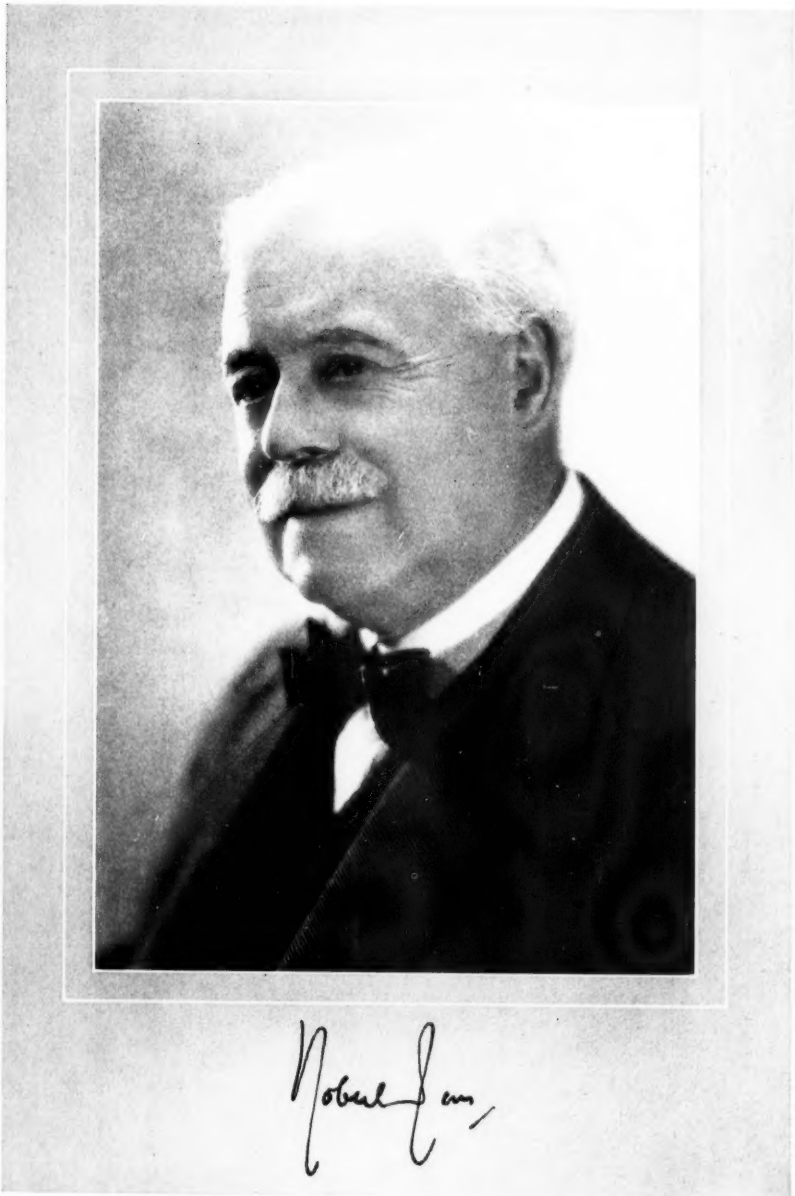
SIR ROBERT JONES

ON January 14, 1933, surgery sustained a great loss in the death of Sir Robert Jones. Certainly no British surgeon ever had greater influence on American orthopedic surgery than he.

Robert Jones was born in 1858 in Wales, took the diploma of the Royal College of Surgeons at the early age of twenty, became associated with his uncle, Hugh Owen Thomas, the son of a famous bone setter, a man of rare ability and the originator of the Thomas splint, and soon was appointed to the surgical staff of the Royal Southern Hospital of Liverpool. Hugh Owen Thomas' private and charity practice was very large and chiefly industrial. It was therefore not strange that, although Sir Robert's efforts were at first along general surgical lines, his practice ultimately became so predominantly orthopedic that he found it necessary to limit it to that specialty. Thus was established the most interesting orthopedic clinic in Europe.

Although the work of Jones was well known early by the small group of surgeons comprising the American Orthopedic Association, it was not until 1907 that American surgeons as a whole appreciated the remarkable work he was doing. The interest of these men was awakened by William J. Mayo who, in 1907, following one of his many journeys abroad forcibly called attention to what was going on in Liverpool. He said: "Just as Lawson Tait carried sound surgery into the abdomen, and Mr. Victor Horsley into the cranial cavity, so has Mr. Jones carried sound surgical principles into orthopedic practice, and rapid cures are the result in a large number of cases in which treatment had been given for months and years by orthopedic apparatus. This does not mean that Mr. Jones has discarded these measures. He is most careful in the after treatment and uses mechanical contrivances for their proper purposes as an adjunct to surgery, not in place of it. . . . All operations are done under ether anæsthesia. The asepsis is most painstaking and thorough. He is expeditious, yet neglects not the smallest detail and his wonderful experience enables him to do wizard-like operations with a precision that is startling. So unassuming and modest is the man that he is, I believe, entirely unaware of his great ability." Sir Robert's operations were models of technical skill, and his plans of treatment examples of an orderly attack on the problem to be solved. One soon discovered that his real enthusiasm was for the ultimate result to be achieved and not for the brilliance of the actual operation. The ease with which he would perform fifteen to thirty operations in an afternoon was astonishing.

As the years went by many honors came to him. He was knighted in 1917; two years later was appointed Knight of the British



Empire, was elected to fellowship in the English and Irish College of Surgeons and also received the American Distinguished Service Order. He received the F. R. C. S. (Edinburgh) in 1889. The Universities of Wales, Aberdeen, Liverpool, Harvard, and Yale gave him honorary doctorates and the American College of Surgeons elected him an honorary fellow.

When the war broke out in 1914 and the British hospitals were soon filled to overflowing with the injured sent home from France, many of the surgeons of the country were in service abroad and the organization for the care of this large number was totally inadequate. The government called on Sir Robert to take charge, and he immediately rose to meet the situation. He segregated the cases and developed the personnel for their care. The first center established was Shepherd's Bush, London, and in this effort he called on his American colleagues to come to his aid. He was able gradually to establish many other military orthopedic hospitals until there were finally 33,000 beds given over to orthopedic service in England. Following the war, Sir Robert exerted his energies for the prevention and cure of crippling diseases and was first chairman and later president of the Central Council for the Care of the Cripple.

On his seventieth birthday a volume of collected essays was presented to him as an assurance of the high esteem in which he was held by his colleagues and former pupils.

As a teacher he was pre-eminent, not in the rôle of the didactic pedagogue, but in the rôle of a leader able to enthuse men, and through them he advanced the art and science of his specialty. During his busy years Robert Jones was thinking, and by speech, writing, and clinical teaching, he inspired many. His contributions to orthopedic surgery were numerous and his *Text Book of Orthopædic Surgery*, written in conjunction with his old friend the late Robert Lovett, is much used in America.

Sir Robert's success cannot be explained by mere achievements in the realm of surgery. His personality was remarkable; the spark of real genius existed in a man of great physical endurance, with a well balanced outlook on life. These attributes brought him fame and renown, and one only had to know him to realize that they also brought him happiness.

In the preface to the birthday volume mentioned, Lord Moynihan wrote in his inimitable style: "Few men have ever possessed in so radiant a degree the genius for friendship. No one can be long in his company, none can work with him or play with him, without realizing not only the sweet simplicity of his character, but the greatness of his heart. . . . In a long and very intimate friendship I have never heard an unjust criticism, a cruel gibe, or a word of bitter cynicism on his lips. His personality radiates cheerfulness, good temper and good will."

In 1911, following in the footsteps of many others, it was my good fortune to visit Sir Robert. I landed at Liverpool on Saturday, and decided to attend his usual Sunday morning free clinic. On setting out from the old Adelphi Hotel, I inquired how to reach 11 Nelson Street, and was given the general direction and told that I could not miss it for I would see the lame and the halt with their crutches and canes making their way to the great physician. Thus guided I easily found my way and on entering the building and making myself known I was taken immediately to Sir Robert and introduced to him. I have never forgotten the cordial friendly welcome accorded me and the ease with which I was fitted into the routine of a busy clinic in a few days. I was given a white coat to wear and was introduced to Sir Robert's patients as his American assistant. That first Sunday

morning I was astounded at the large number of patients he saw, all charity, and the large percentage that he actually did something for on the spot. Malunited fractures, not yet solidified, were straightened, club feet were manipulated, bow legs of babies fractured, straightened, and splinted, and stiff shoulders with periarticular adhesions manipulated. All this was done without anæsthesia and so quickly was it done under the spell of the man's personality that it seemed incredible.

The several months that I spent in daily contact with Sir Robert Jones are among the most enjoyable of my professional career. Another young American, Dr. Henry Fitzsimmons, a pupil of Robert Lovett of Boston, was there at the same time and we enjoyed together the rare privilege of association with this master. We were taken with him on his visits to Heswall, on the banks of the river Dee where the new Children's Hospital was situated, and to Baschurch where there was at that time a primitive sort of a hospital with open air shelters. This hospital was presided over by a remarkable woman of unusual force and character, Dame Agnes Hunt, a former patient of Sir Robert. The Baschurch Hospital later became the prototype of the Cripple's Hospitals in England. In the private clinic at 11 Nelson Street where we were in daily attendance Sir Robert was never too busy to take the time to show us the interesting cases, explaining the problems presented in each case, and always emphasizing the point in the case that was important. He radiated energy, friendliness, and kindness, and his patients came immediately under the spell of his personality. If the so called art of medicine was ever personified in its highest form in one individual it was in Sir Robert Jones. With all the very apparent high idealism that prevailed in his clinic one might expect aloofness and dignity, but on the contrary there was softening humor and humaneness that was delightful. Never did we hear criticism of a colleague or of previous treatment. The correct diagnosis and treatment would be outlined, but nothing derogatory of previous efforts was ever mentioned, no matter how richly, to our younger minds, it seemed deserved.

In 1918, he suffered a great and almost crushing loss in the death of his wife. Their family life was ideal. Lady Jones was his companion in his life work, and many recall the delightful hospitality that was extended to those fortunate enough to visit in their home. Sir Robert lived to the age of seventy-four in full health and surprising vigor up to within a few months of his death. He is survived by a son, a member of the bar, who succeeds to the title, and by a daughter. The news of his death came as a shock to his many American friends, for he seemed to have perpetual youth and one simply could not think of him as growing old. His death came as we all would have wished it for him, quietly and quickly.

M. S. HENDERSON.

HOW SHALL WE TREAT BRAIN ABSCESSES?

NOT many years ago there would have been but one answer to that question—evacuation and drainage. There was little variation in the technique, the operation was performed once an abscess was suspected and localized, and the mortality was distressingly high. Since the Great War, and more particularly during the past ten years, the subject has been given more intensive study. More attention has been paid to the histopathology of brain abscess, more techniques have been proposed, and there prevails today a much clearer understanding of the problems involved—diagnosis, localization, treatment. Of these three we will consider only the treatment. Under treatment there are two major questions: when to operate and how to drain. There is no doubt that many of the failures of the past should be charged to ill timed operations, operations undertaken before the abscess was thoroughly encompassed by a well organized capsule. *We must acknowledge that an abscess in the making is not a surgical lesion.* To be master of the situation, the surgeon's mind must be continually focused on the process of encapsulation. It is reasonably safe to assume that fibrous encapsulation, that is the transformation from the migrating lymphocytes into fibroblasts and mature connective tissue, requires at least three weeks. The process of encapsulation is by no means uniform as to time. In some cases, for reasons unknown, the development of the connective tissue elements proceeds more slowly than in others. *The question constantly before the operator is not "how soon can I operate," but rather "how long is it safe to defer operation."* It is here that the operator's judgment is taxed to the utmost, and, since so often the actual date of the primary infection is undetermined, the operator must be guided chiefly by the signs of increased intracranial pressure, particularly headache and papillœdema.

According to Lillie[1] attempts at drainage should be deferred until the choking has attained its maximum and the discs have become quiescent. Quite recently Woltman,[2] as a guide to the degree of encapsulation, advocates a study of the cellular elements of the cerebrospinal fluid. There is no ground, he says, for the traditional fear of lumbar puncture in the presence of a brain abscess. If the neutrophils are present he assumes that encapsulation is not progressing satisfactorily. When, however, the lymphocytes in the cerebrospinal fluid predominate, he assumes the conditions for operation are more favorable. If these observations of Woltman are generally accepted we will have the only specific guide as to when the operation should be performed. At all events *an operation, premature, usually spells disaster. Procrastination may lead to disaster by rupture of the abscess into the ventricles or by a foraminal hernia.*

During the past ten years three radically different procedures have been practiced: (1) the conventional tubular drainage; (2) drainage by the King method[3] in which unroofing and herniation are the principal features; (3) repeated evacuation as practiced by Dandy.[4] The King method has claims to originality, but statistics are not available to permit of its evaluation. Repeated evacuation by the Dandy method should be given preference, at least when the pus contains no organisms and in small deep seated abscesses. Coleman[5]

[1] Acta oto-laryngol., 1927, 11, 479.
[2] J. Am. M. Ass., 1933, c, 10.
[3] Surg., Gynec. & Obst., 1924, xxxix, 554.
[4] J. Am. M. Ass., 1926, October 30.
[5] J. Am. M. Ass., 1930, xcv, 568.

recommends a subtemporal decompression, synchronous with tapping, to prevent the ill effects of a secondary rise of intracranial pressure.

We have been impressed with the writings of Coleman (loc. cit.) and with the results which he obtained in his series of 28 cases. Coleman prefers drainage with a soft rubber catheter as inflicting the minimum degree of trauma. The catheter is allowed to remain *in situ* until extrusion takes place. For the present, one or the other of these two methods, that of Coleman or Dandy, must be accepted as the method of choice.

We must not forget, as reminded by the title of an article by Globus and Horn,[1] "Inherent Healing Properties of Abscess of the Brain," that there are certain instances in which these "inherent healing properties" may continue until resolution is complete. Again there are certain cases in which the abscess wall is so firm that the operator has removed the lesion *in toto* in the belief that he was dealing with a neoplasm. With this in mind, the question at once arises, will the time come when this method will become the accepted procedure. The final pronouncement cannot be made until there have been assembled reasonably large series of cases treated by one or the other of these methods. But the reader will have gathered from the tenor of these remarks that the tendency of the day is away from the early operation and toward procrastination until encapsulation is secure. It may be as time goes on, by repeated tapping or complete excision, fewer lives will be lost from rupture of the abscess or from the effects of increased pressure—the consequence of delay—than now are lost by attempts at drainage earlier in the course of the disease.

CHARLES H. FRAZIER.

[1] Arch. Otolaryngol., xvi, 603–660.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN a foreword we are told "These *Archives of Obstetrics and Gynecology*[1] are to be made up of contributions by the outstanding men of America, chiefly heads of departments and prominent teachers in our leading medical schools"; and "this work will be the first chapter in the continued history of what America has to tell about obstetrics and the diseases of women." It is planned to publish a new edition every five or eight years, and a new editor is to be chosen from time to time, in order that this work may secure a continuous and permanent place in our Literature.

In such a way the general scheme of this large undertaking is outlined before us. As its syllabus indicates, the contributions are in reality a series of monographs, written by their respective authors, and yet at the same time influenced, modified, and integrated into a system under the supreme authority of the editor himself.

Accordingly there is implied here, not only the individual labor but also a co-operation and a teamwork as between the contributors themselves; "the result of many conferences and unselfish good-will." This quotation indicates the special kind of editor who has inspired and controlled this publication.

The work is to appear in three volumes, each of some eleven hundred pages. Dr. Franklin H. Martin, in an introductory chapter, entitled "The New Surgical Literature," speaks of it as, "An encyclopedia of obstetrics and gynecology," and prophesies that "it will become an inspiration to the specialist, a guide to the independent practitioner, a model for teachers, and a comprehensive textbook for advanced students." Certainly no publication of such magnitude, dealing with these two subjects, has been undertaken since the appearance, in 1924-29 of *Biologie und Pathologie des Weibes*, in eight volumes, by Professors Halban and Seitz. It is true that in England, *The Practitioner's Encyclopedia of Midwifery and the Diseases of Women*, edited by John S. Fairbairn, was published in 1921, while later, in 1924 there was added a textbook, *Gynæcology with Obstetrics*, written by Dr. Fairbairn himself. In Scotland, in 1923, *A Combined Text-book of Obstetrics and Gynæcology*, was issued by Professor Munro-Kerr and Drs. J. Haig Ferguson, J. Young, and J. Hendry. These British publications, however, are comparatively small, and were written specially for the undergraduate student.

No one has plead more eloquently than Dr. Fairbairn for the natural and organic union that should exist between these two subjects of obstetrics and gynecology; and no one will welcome more cordially than he this union, as exemplified in these present *Archives*. In the introduction to his own *Encyclopedia* he pronounces the two subjects as one and indivisible, and quotes the words of John Calvin: "It is a dull and obtuse mind which divides in order to distinguish, but it is a still worse which distinguishes in order to divide."

There certainly is nothing of division in our welcome to this American *Encyclopedia*.

The first volume has just appeared, and it is of this that we now speak.

Naturally this first volume deals with the anatomy of the female genital tract, and with the physiology of these reproductive organs; special sections are devoted to the morphology and the physiology of pregnancy, to the physiology of the birth processes, to labor, and a final section to the pathology of pregnancy.

"The Anatomy of the Female Genitalia and Pelvic Soft Parts" has been written by Barry J. Anson, associate professor of anatomy, Northwestern University, Chicago. While the descriptive text is clear and succinct, it is greatly strengthened by the original drawings, which have been made by W. Branks Stewart, under the author's supervision. These drawings show originality, both in conception and execution, and it is evident that they have been prepared with great care. An editor's note informs us that every effort has been employed to correct the inevitable distortion of postmortem dissections, by a painstaking comparison of measurements, taken in the living subject during pelvic operations.

Fred L. Adair, professor of obstetrics and gynecology, University of Chicago, has long been recognized as an authority upon the bony pelvis. In this chapter, "The Bony and Ligamentous Pelvis," he naturally deals first and chiefly with this subject from the obstetrical point of view. Fortunately, however, he has added to this description many interesting details concerning the ontogeny and phylogeny of this weight-bearing girdle. The pages that deal with the ossification and development of this bony pelvis are worthy of special mention.

Emil Novak, of Johns Hopkins University, writes of the "Physiology of the Reproductive Organs (exclusive of Pregnancy)" and no one could do it better. This physiology is really embraced and included in the function of menstruation, its me-

[1] OBSTETRICS AND GYNECOLOGY. Edited by Arthur Hale Curtis, M.D. Vol. i. Philadelphia and London: W. B. Saunders Company, 1933.

narche, its menacme, and its menopause. The cyclical changes in the genital canal associated with menstruation are clearly described, the illustrations are well chosen, and have been clearly reproduced. Novak is here writing on his own special subject.

There follows a chapter on "Menstruation in the Light of the Newer Knowledge concerning the Physiology of Reproduction," written by Novak, and Carl G. Hartman, of the Carnegie Laboratory of Embryology, Johns Hopkins University. We specially commend this chapter, dealing as it does with the modern endocrine viewpoint of the physiology of menstruation; and also a most interesting description of "The Reproductive Cycle in Animals," written by Hartman himself. We gladly endorse the tribute paid to Marshall's hand-book *The Physiology of Reproduction*, its second edition, published ten years ago, as "a mine of references . . . and a most useful initial guide to wider reading."

The chapters on "Morphology and Physiology of Pregnancy" are among the strongest in the book; in especial those dealing with "Maturation and Fertilization of the Ovum," "The Early Development of the Embryo," and the chapter on "Placentation, Fetal Membranes, and Deciduae." Professor Bradley Patten, of Western Reserve University, Cleveland, and Carl G. Hartman, of Baltimore, "have surely made," in the words of the editor, "a great team." The photomicrographs of the fertilized and living ovum of the monkey, showing its cleavage divisions, and its growth changes, are the best that we have seen. In micro-moving pictures, these cleavage divisions begin with the two cell stage, and are carried on to the eight cell stage, 49 hours and 48 minutes after ovulation. In this way the morula stage is reached. The blastula changes are shown, from living embryos of the rabbit, with the formation of the blastocele and the inner cell mass, which carries us by a single hypothetical stage to the condition of the human embryo, 10 to 11 days after fertilization, in the famous Miller embryo, as described by Streeter. In this way and by these stages, the initial chapter of the life history of the human embryo has been wonderfully depicted.

"Placentation, Fetal Membranes, and Deciduae" are described by Professor Leslie Brainerd Arey, Northwestern University Medical School. He describes the early penetration of the uterine mucosa by the guinea pig ovum, and passes directly to a description of the embedded human embryo of Miller, Bryce Teacher, and Peters. Of the fetal membranes it is interesting to observe that the amniotic cavity is already formed in the Miller embryo, probably by a splitting of the ectodermal cell mass. Further than this assumption, even yet, we are not permitted to go. It is a pleasure to read these pages of Professor Arey, for the scientific description is not only well illustrated, but is charged with items of clinical value and importance.

There follow interesting chapters on "Diseases of the Embryo and Appendages," by Professor A. Schumann, and one on "Maternal Changes Incident to Pregnancy," by J. Isfred Hofbauer, of Johns Hopkins University; but space forbids anything more than a mention of these.

"The Diagnosis of Pregnancy and its Management" are well up to the level of our standardized textbooks, and admittedly this standard is high. The same may be said of the section of "Labor." In the "Conduct of Normal Labor," Professor Joseph Baer of Rush Medical College, University of Chicago, speaks of delivery in the left lateral position as a method which has not received sufficient recognition in America. We think this statement is true. To the several advantages of this position, enumerated in the text, we would add one other; namely, its great usefulness in a private house, where hospital facilities, and assistants are few, or wanting altogether.

Professor Patten makes a definite contribution to our knowledge of "Changes in the Fetal Circulation Following Birth." He adds the key-stone to the arch of our understanding of, the gradual closure of the foramen ovale; the antenatal and neonatal pulmonary circulation; and the active histological changes at work in the closure of the Ductus arteriosus.

Our interest in "The Pathology of Pregnancy" naturally centers around the toxæmias. This chapter has been contributed by Robert D. Mussey and Lawrence M. Randall, of the Mayo Clinic. These authors have successfully resisted the modern temptation of loading their pages with too much of theory, and have confined themselves happily to clinical distinctions. Their sharp separation of chronic nephritis from the true toxæmias will meet with approval; and also their general recommendations concerning antenatal care, early diagnosis, and treatment.

No review of this first volume would be complete without a special reference to the early chapter, "Historical," written by Irving S. Cutter, dean, Northwestern University Medical School. This monograph is a well balanced summary of the history of obstetrics and gynecology, in Great Britain, France, Germany and America. Clearly conceived and written, it provides the reader with an excellent introduction to the work before him.

The volume itself has been well produced, both in its text and illustrations.

We congratulate Dr. Curtis, his contributors, and his editorial staff. W. W. CHIPMAN.

AN unusual book; in some respects an extraordinary book; an extraordinarily good book is *Peripheral Nerve Injuries*[1] by Pollock and Davis. The assembled material is nowhere else duplicated and I am inclined to doubt that there are anywhere two other men who could duplicate it.

[1] HOEBER'S SURGICAL MONOGRAPHS. PERIPHERAL NERVE INJURIES. By Lewis J. Pollock, M.D., and Loyal Davis, M.D. New York: Paul B. Hoeber, 1933.

That every neurological surgeon and every neurologist will soon possess this monograph (678 pages) is obvious. Assuredly every industrial surgeon should have it. If and when we have another war it will become a *vade mecum*. In fact any physician who has to do with peripheral nerve injuries will find himself in need of this comprehensive manual. The following will convey an idea of the contents.

After a brief chapter on the incidence of peripheral nerve injuries, nine fertile chapters (97 pages) are devoted to "Examination." They include a lot of symptomatology, especially relating to overlap and sensory dissociation. That is, one is told what to look for, how to look for it, what one finds and how to interpret the findings.

Follow three valuable chapters (27 pages) on "Diagnosis" wherein the chaff is blown from the wheat: theory rendered negative by the facts of experience. Chapter XIV is peculiarly lucid and contains all that any clinician needs to know of the development and structure of peripheral nerves. In Chapters XV and XVI the authors very adequately cover the pathology of peripheral nerve lesions and the fascinating processes of nerve degeneration and regeneration—almost a *terra incognita* to the ordinary run of physicians and surgeons.

In Chapter XVII will be found explicitly set forth the indications—and contra-indications—for surgical treatment: dicta rational as well as explicit and in the following one brief descriptions of nerve transplants or grafts, nerve implants, nerve crossing, nerve flaps, suture à distance, tubular suture and end-to-end suture.

The technique of the various surgical procedures for nerve repair is very clearly described in 24 pages (Chapter XIX) and statement of what should be and can be done in the way of after-treatment follows. As quite germane to the subject in hand tendon transplantation, neurotization of paralyzed muscles and immobilization of joints are summarily considered in Chapter XXI.

Pages 264 to 544 are devoted to the symptomatology, diagnosis, and treatment of injuries of the various individual nerves, including the brachial and other plexuses and multiple lesions; and what these pages contain is bound to become classic medical literature. For instance, the 34 pages on the radial nerve and its injuries constitute a veritable mine of authentic information and sound counsel. They leave nothing essential to be said. The same applies to the text on the other nerves. The matter is based on extensive experience, accurate observation, full knowledge of the work of others and sound judgment. It is especially to be noted that the choice of operative procedure receives mature consideration and that operative technique is presented in detail.

Finally, there is a very instructive chapter on the results of peripheral nerve surgery. It contains a vast amount of information but lacks the personal opinion—or impression—of the authors.

The text is followed by a colossal bibliography (1958 titles), a monument to someone's untiring industry and meticulous care. Then a full index of authors with page references and a subject index which should put European authors and publishers to shame.

The illustrations are unexcelled, mostly original, some of them beautiful, and they really illustrate.

In the presence of so many major excellencies it is painful to note a considerable number of minor blemishes—easily to be removed in a second edition. Frequently the English is loose, sometimes even inaccurate or vague. Weir Mitchell's first name is misspelled at least seven times, three times on one page. On page 257 the text does not agree with the legends of the illustrations. There is some needless duplication of statement and some scores of articles (a and an) might well be deleted.

HUGH T. PATRICK.

WRITTEN primarily for roentgenologists and based on 209 verified tumors, *Intracranial Tumors*[1] is quite complete. The types of Intracranial tumors are well classified and some are dealt with in detail. The second chapter, dealing with direct roentgenological evidence of intracranial tumors, is well written and covers the field very satisfactorily, especially the pineal gland calcification and the importance of a shift in its position.

Chapter three, dealing with meningiomata, classifies these tumors regionally, describes them roentgenologically, pathologically, and enumerates symptoms. The origin of meningiomata is brought out very clearly. The case reports throughout the book are very concise and clear, also the operative and postmortem findings are given in a quite complete manner. Davis divides meningiomata into two groups, (1) massive, roughly spherical, and (2) flat, slightly elevated.

Hypophyseal adenomata are covered in chapter four. The tumors are classified according to their staining characteristic, namely, chromophobe, chromophil, and basophilic. The chromophobe are the commonest, the chromophil the next in order and the basophilic adenomata are comparatively rare. The symptoms and clinical findings are usually diagnostic of the types of adenomata, namely, chromophobes with hypopituitarism and chromophil with hyperpituitarism. The X-ray findings are often of great value in the diagnosis of hypophyseal adenomata. The ballooned-out type of erosion is quite characteristic of intrasellar tumors. The findings must be closely studied as other types of extrasellar tumors often cause changes in the sella and clinoid processes. Other X-ray findings are also described, such as large supra-orbital ridges, thick skull, large external occipital protuberance and the prominent jaw.

Acoustic neurinomata and craniopharyngiomata are covered in chapters five and six. The X-ray

[1] ANNALS OF ROENTGENOLOGY: A SERIES OF MONOGRAPHIC ATLASES. Edited by James T. Case, M.D. Vol. xiv, INTRACRANIAL TUMORS. By Loyal Davis, M.D., Ph.D. New York: Paul B. Hoeber, Inc., 1933.

findings in acoustic neurinomata are in and about the porus acusticus. Usually the changes are of a destructive character. Positions best to show these areas roentgenologically are described. The craniopharyngiomata are tumors of childhood or early adult life. They are congenital and are usually located in the hypophyseal region—"Rathke's pouch." These tumors are very frequently calcified and therefore give direct X-ray findings. The areas of calcification are usually located above and anterior to the sella, although occasionally deposits may be found in the sella. Both types of tumors, acoustic neuromata and craniopharyngiomata are covered very completely in the book.

In chapter seven the gliomata, osteomata, and angiomata are described giving case reports and a few X-ray illustrations. The gliomata give very little direct X-ray evidence, due to the fact they are not often calcified nor do they show calcified deposits. The osteomata and angiomata are not described in detail, but the important points are well brought out.

The chapter on ventriculography and encephalography is very complete, reviewing the literature and describing the various methods used in both ventriculography and encephalography. The ventricular pathways are completely described and the causes of changes in the pathways are enumerated. The author gives a sign of warning which is important, namely, try to make a diagnosis by the older methods before subjecting the patient to either ventriculography or encephalography. Each method is a surgical procedure and should be reserved for a patient with an unlocalized lesion and then only in a hospital under the best surgical conditions.

The last chapter on radiation therapy of intracranial tumors reviews the literature and gives the views of many radiologists and neurologic surgeons, plus the technique used by the author. The effects of radium and X-rays on brain tissue is discussed, with warnings not to use large doses (above 1,000 r) at one seance. Headaches, œdema and hyperæmia often follow large doses of irradiation.

The book, I believe, fills a much needed space in a rather new but rapidly growing field of surgery. The book is well written, in rather large type, and is interesting to read.

Our only criticism is that the X-ray reproductions are not clear and many of the areas mentioned in the text and legends are very difficult, and in some instances impossible to find. It is our belief that too many conclusions are drawn from the X-ray reproductions. It is possible that the conclusions drawn from the X-ray findings were very evident on the original films but could not be plainly reproduced on prints. EDWARD L. JENKINSON.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

INTRACRANIAL TUMORS. By Percival Bailey. Springfield, Illinois, and Baltimore: Charles C. Thomas, 1933.

A SURGEON'S POCKET BOOK. By H. S. Souttar, D.M., M.Ch.(Oxon.). London: William Heinemann Ltd., 1933.

ZANGENGEBURT IM ROENTGENBILD. By Dr. Werner Luettge. Munich: Ernst Reinhardt, 1933.

LIGHT THERAPY. By Frank Hammond Krusen, M.D. New York: Paul B. Hoeber, Inc., 1933.

ANNALS OF ROENTGENOLOGY. Edited by James T. Case, M.D. Vol. x. PEPTIC ULCER. By Jacob Buckstein, M.D. 2d rev. ed. New York: Paul B. Hoeber, Inc., 1933.

OPERATIVE SURGERY; THE OPERATIVE TECHNIC INVOLVED IN THE OPERATIONS OF GENERAL AND SPECIAL SURGERY. By Warren Stone Bickham, M.D., and Calvin Mason Smyth, Jr., B.S., M.D. Vol. vii. Philadelphia and London: W. B. Saunders Company, 1933.

ABORTION: LEGAL OR ILLEGAL? By A. J. Rongy, M.D., F.A.C.S. New York: The Vanguard Press, 1933.

SURGICAL OPERATIONS; FOR STUDENTS AND NURSES. By E. W. Hey Groves, M.D., B.Sc., M.S., F.R.C.S. 3d ed. New York and London: Oxford University Press, 1933.

BINOCULAR VISION AND THE MODERN TREATMENT OF SQUINT. By Margaret Dobson, M.D.(Lond.). London: Oxford University Press, 1933.

THE PRINCIPLES OF TREATMENT OF MUSCLES AND JOINTS BY GRADUATED MUSCULAR CONTRACTIONS. By Morton Smart, C.V.O., D.S.O., M.D., Ch.B. (Edinb.). London: Oxford University Press, 1933.

OPERATIVE SURGERY. By Alexander Miles, M.D., LL.D., F.R.C.S.Ed. and D. P. D. Wilkie, M.D., F.R.C.S. Ed. and Eng. London: Oxford University Press, 1933.

THE NERVOUS CHILD AT SCHOOL. By Hector Charles Cameron, M.A., M.D.(Cantab.), F.R.C.P.(Lond.). London: Oxford University Press, 1933.

INHERITED ABNORMALITIES OF THE SKIN; AND ITS APPENDAGES. By E. A. Cockayne, D.M., F.R.C.P. London: Oxford University Press, 1933.

FORTSCHRITTE AUF DEM GEBIETE DER ROENTGENSTRAHLEN. Edited by Prof. Dr. Grashey. Vol. xliv. DIE KOMBINIERTE ENZEPHAL-ARTERIOGRAPHIE. By Prof. Dr. W. Loehr, Prof. Dr. W. Jacobi. Leipzig: Georg Thieme, 1933.

LES VOIES DE PÉNÉTRATION DES MEMBRES. Tome ii. MEMBRE INFÉRIEUR. By F. M. Cadenat. Paris: G. Doin & Cie, 1933.

ELEMENTARY HANDBOOK ON RADIUM etc. By D. F. Clephan, H. M. Hill. London: Oxford University Press, 1933.

ROENTGENOGRAPHIC STUDIES OF THE URINARY SYSTEM. By W. E. Lower, M.D., F.A.C.S., and B. H. Nichols, M.D., F.A.C.R. St. Louis: The C. V. Mosby Company, 1933.

THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY. Vol. iv. NONTRAUMATIC SURGERY. New York and London: D. Appleton and Company, 1933.

VORBEUGUNG UND BEKAEMPFUNG DER OPERATIONSGEFAHREN. By Prof. Dr. M. Kappis. Leipzig: Georg Thieme, 1933.

A NEW APPROACH TO DIETETIC THERAPY; METABOLISM OF WATER AND MINERALS AND ITS DISTURBANCES. By Eugene Foeldes, M.D. Boston: Richard G. Badger, 1933.

THE PHYSIOLOGICAL EFFECTS OF RADIANT ENERGY. By H. Laurens, Ph.D. American Chemical Society Monograph New York: Chemical Catalog Company, Inc., 1933.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

J. Bentley Squier, New York, *President* William D. Haggard, Nashville, *President-Elect*
Franklin H. Martin, Chicago, *Director-General*
Philip H. Kreuscher, *Chairman;* Oscar E. Nadeau, *Secretary, Committee on Arrangements*

PRELIMINARY PROGRAM FOR THE CLINICAL CONGRESS IN CHICAGO

IN the following pages appears a preliminary program of operative clinics and demonstrations to be given in the hospitals and medical schools of Chicago during the twenty-third annual Clinical Congress of the American College of Surgeons, October 9–13, 1933. It will be noted that clinics are scheduled to begin at 2 o'clock on the afternoon of Monday, October 9, and to continue during the four following days both morning and afternoon. All departments of surgery will be represented in the clinical program—general surgery, gynecology, obstetrics, urology, orthopedics, proctology, and surgery of the eye, ear, nose and throat.

The clinical program is being prepared under the supervision of the Committee on Arrangements appointed by the Board of Regents, which Committee is comprised of the members of an Executive Committee—Philip H. Kreuscher, chairman; Oscar E. Nadeau, secretary; Joseph Beck, William R. Cubbins, Frederick H. Falls, Harry S. Gradle, Carl A. Hedblom, Charles E. Kahlke, Herman L. Kretschmer, Karl A. Meyer, Dallas B. Phemister, Edwin W. Ryerson, and Henry Schmitz—together with representatives of each of the hospitals and medical schools cooperating in the clinical program.

The surgeons of Chicago are keenly interested to present a program of clinics and demonstrations that will provide a complete showing of this city's clinical activities in all departments of surgery. The Committee on Arrangements in making their plans has been assured of the hearty co-operation of the clinicians in the medical schools and more than fifty hospitals that will participate in the clinical program. The Committee is planning for a number of special features in the clinical program to include: (1) Demonstrations at several hospitals of modern methods in the treatment of fractures; (2) cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray; (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation by surgery and physiotherapy of patients injured in industrial, automobile and other accidents.

Two sub-committees have been appointed to supervise the program for the sections on surgery of the eye, ear, nose and throat as follows: Ophthalmology—Harry S. Gradle, chairman; Thomas D. Allen, E. K. Findlay, Sanford Gifford. Otolaryngology—Joseph Beck, chairman; Austin A. Hayden, Edward P. Norcross, S. J. Pearlman. The recommendations of these committees insure a worth-while program of clinics and scientific sessions for all those interested in these specialties.

This year the College celebrates its twentieth anniversary, the first convocation having been held in Chicago in 1913. It will be recalled that the first Clinical Congress was held in this city in 1910 and was largely attended by enthusiastic surgeons from all parts of the United States and Canada.

SPECIAL FEATURES OF PROGRAM

In a symposium on "Cancer is Curable" on Wednesday afternoon, at 2:30, eminent surgeons of wide experience in varied fields of surgical practice and from all parts of the United States and Canada will present their reports as to cases of cancer cured. A similar symposium at the Congress in St. Louis last year established a new viewpoint with the profession and the laity, and created widespread favorable comment. Among the contributors will be: Irvin Abell, M.D., Louisville; Frank K. Boland, M.D., Atlanta; Malvern B. Clopton, M.D., St. Louis; Charles A. Dukes, M.D., Oakland, Calif.; James Monroe Mason, M.D., Birmingham, Ala.; John T. Moore, M.D., Houston, Texas; Eugene H. Pool, M.D., New York; Richard R. Smith, M.D., Grand Rapids; E. Starr Judd, M.D., Rochester, Minn.;

Brooke M. Anspach, M.D., Philadelphia; William P. Healy, M.D., New York; Martin B. Tinker, M.D., Ithaca, N. Y.; William B. Coley, M.D., New York; Chevalier Jackson, M.D., Philadelphia.

A symposium on urologic surgery will be presented on Friday morning at 11 o'clock, the tentative program for which includes: John R. Caulk, M.D., St. Louis on "Cautery Removal of Prostatic Obstruction"; Frank Hinman, M.D., San Francisco, "The Pathogenesis of Hydronephrosis"; Joseph F. McCarthy, M.D., New York, "The Prostate Gland—Its Place in General Medicine; Newer Conceptions of Diagnosis and Therapy."

Other important features of the general program for the Congress include: (1) Conference on fractures arranged by the College Committee on the Treatment of Fractures to be held on Tuesday afternoon; (2) a symposium under the auspices of the Board of Industrial and Traumatic Surgery on Friday afternoon; (3) a symposium on teaching of surgery and surgical specialties on Thursday afternoon following the annual meeting.

EVENING MEETINGS

Programs for a series of five evening meetings to be held in the Ballroom of the Stevens Hotel are being prepared by the Central Executive Committee of the Congress. At the Presidential Meeting on Monday evening Dr. Philip H. Kreuscher, chairman of the Committee on Arrangements, will welcome the visiting surgeons to Chicago, followed by Dr. Franklin H. Martin, Director-General of the College, who will introduce visiting surgeons from foreign countries, a large number of whom have been specially invited to attend the Congress this year. Among these will be Lord Moynihan of London, well known to most American surgeons. The address of the retiring president, Dr. J. Bentley Squier, of New York, will be followed by the inauguration of the president-elect, Dr. William D. Haggard, of Nashville, Tennessee. The John B. Murphy oration in surgery will be delivered at this session by Dr. Loyal Davis, of Chicago.

The 1933 class of candidates will be received into Fellowship in the College at the annual convocation on Friday evening. On this occasion Dr. William D. Haggard will deliver the presidential address, and Robert Maynard Hutchins, A.M., LL.D., president of the University of Chicago, the Fellowship address.

Distinguished surgeons of the United States and Canada, with visiting surgeons from foreign countries, have been invited to present papers dealing with surgical subjects of timely interest at sessions on Tuesday, Wednesday and Thursday evenings. Among the speakers will be the following: George W. Crile, M.D., Cleveland, on "Hyperthyroidism and Associated Diseases"; Edward D. Churchill, M.D., Boston, "Tumors of the Parathyroid Glands"; Howard C. Naffziger, M.D., San Francisco, "Treatment of Exophthalmos"; George E. Brown, M.D., Rochester, Minnesota, "Thrombo-Angiitis Obliterans"; David Edwin Robertson, M.B., Toronto, "Sympathectomy in Children"; Mont Rogers Reid, M.D., Cincinnati, "Some Aspects of Vascular Diseases"; Edgar L. Gilcreest, M.D., San Francisco, "The Common Syndrome of Rupture, Dislocation and Elongation of the Biceps Brachii; with an Analysis of Over Forty Cases."

Papers and discussions on subjects of special interest to ophthalmologists and otolaryngologists will be presented at two sessions on Tuesday and Thursday evenings.

THE HOSPITAL CONFERENCE

The opening session of the Congress—the annual hospital conference—will be held in the ballroom of the Stevens Hotel Monday morning beginning at 10 o'clock. An interesting program of papers, round table conferences and practical demonstrations dealing with the problems related to hospital efficiency is being prepared for this conference, which will continue on Tuesday and Wednesday. Through a careful selection of the subjects to be presented by eminent surgeons and hospital executives, the College aims to make this year's program of wide interest and practical character—particular emphasis being directed toward professional standards and the vital problems related to medical economics. In recent years a greatly increased interest on the part of surgeons in both administrative and scientific phases of hospital work has been evidenced, and for this reason the program to be presented will be unique and provide discussions of importance to the three major hospital groups—medical, surgical and administrative. An opportunity will be afforded to all those interested in the scientific work of the hospital to participate in a program that pertains to the many and varied problems connected with the care of the patient.

HEADQUARTERS—HOTELS

General headquarters for the Clinical Congress will be established at the Stevens Hotel, located on Michigan Avenue between Seventh and Eighth Streets. This hotel affords unusual facilities for all activities of the Congress, as will be remembered by those who attended the Congress in

Chicago in 1929. The grand ballroom on the second floor with other large rooms on the third floor and the exhibition hall have been reserved for the exclusive use of the Congress. All of the evening sessions, the hospital conference on Monday, the annual meeting, the cancer and fracture symposia will be held in the grand ballroom. The registration and information bureau, together with the bulletin boards on which will be displayed the daily clinical program will be established in the exhibition hall in the basement, together with the Technical Exhibition.

Chicago has many fine, large hotels, several within walking distance of the headquarters hotel. A list of the hotels recommended by the Committee on Arrangements is presented herewith. While Chicago's hotel facilities are very great and there should be no difficulty in securing first class hotel accommodations, it is advisable for those who expect to attend the Clinical Congress to reserve their hotel accommodations as far in advance as possible, as the Century of Progress Exposition will undoubtedly bring to Chicago a very large number of visitors.

The Technical Exhibition of the Clinical Congress will be located in the Exhibition Hall together with the registration and information bureau. In the same room will be found the bulletin boards on which the daily clinical programs will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals, and publishers of medical books will be represented in this exhibition.

We are assured that the railways of the United States and Canada will grant especially low rates on account of the Clinical Congress in connection with the Century of Progress Exposition in Chicago. Applications for reduced fares for this meeting are pending before the various railway traffic associations.

ADVANCE REGISTRATION

The hospitals of Chicago afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, the attendance will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the results of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Clinical Congress in Chicago will register in advance.

Attendance at all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

CHICAGO HOTELS AND THEIR RATES

	Minimum Rates With Bath	
	Single	Double
Ambassador, North State Street at Goethe	$3.50	$6.00
Auditorium, Michigan Blvd. and Congress	3.50	6.00
Belden Stratford, 2300 Lincoln Park West	4.00	6.00
Belmont, Sheridan Road at Belmont	4.00	5.00
Bismarck, Randolph at LaSalle St.	3.50	5.00
Blackstone, Michigan Blvd. and 7th St.	3.00	5.00
Brevoort, 120 West Madison St.	2.50	3.50
Congress, Michigan Blvd. and Congress	4.00	6.00
Drake, Lake Shore Drive and Michigan	3.00	5.00
Edgewater Beach, 5300 Sheridan Road	4.00	6.00
Great Northern, Jackson and Dearborn	2.50	4.00
LaSalle, LaSalle at Madison St.	2.50	4.00
Morrison, 79 West Madison St.	3.00	4.50
Palmer House, State and Monroe Sts.	3.50	6.00
Pearson, 190 East Pearson St.	3.00	5.00
Stevens, Michigan Blvd. bet. 7th and 8th	3.50	5.00

PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY, PROCTOLOGY, SURGICAL PATHOLOGY, ETC.

COOK COUNTY HOSPITAL

Monday

SUMNER L. KOCH—2. General surgery.
F. H. FALLS—2. Gynecology.
E. J. BERKHEISER—2. Orthopedics.
WILLIAM R. CUBBINS—2. General surgery.
M. DAVISON—2. General surgery.

Tuesday

SUMNER L. KOCH—9. Diagnostic clinic.
AARON KANTER—9. General surgery.
GEORGE DAVIS—9. General surgery.
A. H. MONTGOMERY—9. General surgery.
A. H. CONLEY—9. Orthopedics.
CAREY CULBERTSON—9. Gynecology.
J. O'DONOGHUE—9. General surgery.
HARRY CULVER—9. Urology.
H. JACKSON—9. General surgery.
MARCUS HOBART—9. Orthopedics.
VERNON C. DAVID—9. Diagnostic clinic.
L. C. GATEWOOD—9. General surgery.
J. P. GREENHILL—2. Gynecology.
RALPH B. BETTMAN—2. Surgery in tuberculosis.
E. WARSZEWSKI—2. General surgery.

Wednesday

CHANNING BARRETT—9. Gynecology.
HARRY CULVER—9. General surgery.
V. L. SCHRAGER—9. General surgery.
GEORGE APFELBACH—9. General surgery.
J. G. FROST—9. General surgery.
R. C. SULLIVAN—9. General surgery.
L. L. VESEEN—9. Urology.
FRANK JIRKA—9. General surgery.
R. VAUGHAN—9. General surgery.
PHILIP H. KREUSCHER—9. Orthopedics.
CHARLES M. MCKENNA—9. Urology.
H. ROLNICK—2. Urology.
HARRY CULVER—2. Urology.
GEORGE DAVIS—2. General surgery.
J. R. BUCHBINDER—2. General surgery.
DAVID HILLIS—2. Obstetrical operations.
SUMNER L. KOCH—2. General surgery.

Thursday

PHILIP H. KREUSCHER—9. Orthopedics.
CHANNING BARRETT—9. General surgery.
GEORGE DAVIS—9. General surgery.
R. W. MCNEALY—9. General surgery.
MARCUS HOBART—9. Orthopedics.
D. HORNER—9. Gynecology.
KARL A. MEYER—9. General surgery.
E. W. FISCHMAN—9. Gynecology.
A. H. MONTGOMERY—9. General surgery.
MAX THOREK—9. General surgery.
A. H. CONLEY—9. Orthopedics.
D. H. LEVINTHAL—9. Orthopedics.
JOHN HARGER—2. General surgery.
F. H. FALLS—2. Gynecology.
E. J. BERKHEISER—2. Orthopedics.
RALPH BETTMAN—2. General thoracic surgery.
WILLIAM R. CUBBINS—2. General surgery.

Friday

GEORGE APFELBACH—9. General surgery.
AARON KANTER—9. General surgery.
R. C. SULLIVAN—9. General surgery.
CAREY CULBERTSON—9. Gynecology.
VERNON C. DAVID—9. General surgery.
MARCUS HOBART—9. Orthopedics.
F. G. DYAS—9. General surgery.
J. O'DONOGHUE—9. General surgery.
H. JACKSON—9. General surgery.
L. C. GATEWOOD—9. General surgery.
JOHN HARGER—2. General surgery.
J. R. BUCHBINDER—2. General surgery.
MARSHALL DAVISON—2. General surgery.
E. WARSZEWSKI—2. General surgery.
SUMNER L. KOCH—2. General surgery.

ST. LUKE'S HOSPITAL

Monday

H. E. MOCK, A. REID MORROW and CHARLES SHANNON—2. General surgical operations.
E. OLDBERG—2. Neurological surgery.

Tuesday

H. O. JONES, WILLIAM P. CARLISLE, M. J. KILEY, E. A. EDWARDS and JOHN BREWER—9. Gynecological operations; early human embryo, demonstration.
CARL HEDBLOM and WILLARD VAN HAZEL—9. Thoracic surgery.
H. E. MOCK—2. Reconstructive surgery.
L. L. MCARTHUR and S. W. MCARTHUR—2. General surgery.

Wednesday

L. E. SCHMIDT—9. Urological clinic.
E. W. RYERSON and F. A. CHANDLER—9. Orthopedic operations.
S. C. PLUMMER—9. General surgery.
H. E. JONES and T. L. HANSEN—9. General surgery.
E. W. RYERSON, R. O. RITTER and H. O. SOFIELD—2. Orthopedic operations.
FRANK E. DAVID, C. J. DEBERE and G. V. PONTIUS—2. Rectal surgery.

Thursday

G. DETAKATS—9. Surgery in juvenile diabetes; ambulatory vein ligation of varicose veins.
H. E. MOCK—9. General surgery.
HARRY CULVER—9. Urological clinic.
H. E. MOCK, A. REID MORROW and CHARLES SHANNON—2. Skull fractures.
W. R. CUBBINS—2. General surgery.
H. B. THOMAS and F. W. HARK—2. Orthopedic clinic.

Friday

W. F. LYON—9. Dislocations of the shoulder with fracture of the greater trochanter.
H. POTTS and F. W. MERRIFIELD—9. Oral surgery, operative.
E. W. RYERSON, F. A. CHANDLER and R. O. RITTER—2. Orthopedic clinic.

PASSAVANT MEMORIAL HOSPITAL—NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

Monday

RUDOLPH HOLMES and staff—2. Symposium on hyperemesis gravidarum.

Tuesday

LEANDER W. RIBA—9. The use of the electro-urethrotome in urethral strictures.
ARTHUR H. CURTIS and GEORGE H. GARDNER—9. Gynecological operations.
JOHN A. WOLFER—9. Cholecystitis, carcinoma of the colon.
JACOB R. BUCHBINDER—9. Thyroid surgery.
JOHN S. COULTER—10. Physical therapy.
PAUL B. MAGNUSON—2. Ununited fracture of the neck of the femur, bone graft in the spine.
JOHN A. WOLFER—2. Dry clinic: Alimentation of the critically ill patient by jejunal feedings.
Obstetrical Department—2. Symposium on cardiac diseases; their obstetrical associations.
LOYAL DAVIS, LEWIS J. POLLOCK, HALE HAVEN and DAVID A. CLEVELAND—2. Symposium on neurologic surgery.

Wednesday

HARRY M. RICHTER—9. Thyroid surgery.
LOYAL DAVIS—9. Neurologic surgery.
SUMNER L. KOCH and MICHAEL L. MASON—9. Nerve and tendon surgery of the hand.
JAMES T. CASE—10. Roentgenology.
PHILIP H. KREUSCHER—2. Hip joint surgery.
ALLEN B. KANAVEL, SUMNER L. KOCH and MICHAEL L. MASON—2. Review of twenty years of surgery of the hand.
LEANDER W. RIBA—2. Dry clinic: Prostatic resection.
EMIL D. W. HAUSER—2. Orthopedic surgery.

Thursday

ARTHUR H. CURTIS and GEORGE H. GARDNER—9. Gynecological operations.
JOHN A. WOLFER—9. Cholecystitis; carcinoma of the breast.
JACOB R. BUCHBINDER—9. Abdominal surgery.
JOHN S. COULTER—10. Physical therapy.
PHILIP H. KREUSCHER—2. Shoulder and knee-joint derangement.
RUDOLPH HOLMES and staff—2. Symposium on toxæmias of late pregnancy, renal and hepatic.
CHARLES A. ELLIOTT, WALTER H. NADLER, PAUL STARR, M. HERBERT BARKER, HOWARD B. CARROLL and HOWARD L. ALT—2. Symposium on hepatic disease.

Friday

HARRY M. RICHTER—9. Gastric surgery.
LOYAL DAVIS—9. Neurologic surgery.
SUMNER L. KOCH and MICHAEL L. MASON—9. Irradiation ulcers of the hand, Dupuytren's contracture.
JAMES T. CASE—10. Roentgenology.
PAUL B. MAGNUSON—2. Demonstration of principles for overcoming deformity in ununited fractures before operation; bone grafts for ununited fractures.
RUDOLPH HOLMES and staff—2. Obstetrical hæmorrhages.
HARRY M. RICHTER, ANDREW C. IVY, SAMUEL J. FOGELSON and A. J. ATKINSON—2. Symposium on gastric ulcer.

U. S. MARINE HOSPITAL

Wednesday

O. E. NADEAU—9. General surgical clinic.

Friday

O. E. NADEAU—9. General surgical clinic.

PRESBYTERIAN HOSPITAL

Tuesday

A. D. BEVAN—9. Surgery of the breast.
V. C. DAVID—9. Carcinoma of sigmoid.
H. L. KRETSCHMER—9. Kidney surgery.
R. H. HERBST—9. Transurethral electro resection of prostate gland.
KELLOGG SPEED—9. Tumors of chest wall, demonstration of cases, lantern slides.
A. H. MONTGOMERY—11. Abdominal surgery in children.
A. VERBRUGGHEN—2. Neurosurgical operation.

Wednesday

A. D. BEVAN—9. Hernia and undescended testicle.
F. B. MOOREHEAD—9. Plastic surgery of mouth and face.
C. B. DAVIS—9. Tumors of the large intestine.
H. L. KRETSCHMER—9. Surgery of the bladder.
N. S. HEANEY—9. Vaginal surgery.
DR. GATEWOOD—10. Carcinoma of stomach, follow-up clinic.
E. M. MILLER—10. Thyroid surgery.
H. A. OBERHELMAN—10. Surgery in diabetic patients.
E. R. MCCARTHY—11. Strangulated hernia in infants.
W. J. POTTS—12. Fracture problems.

Thursday

A. D. BEVAN—9. Surgery of gall bladder and bile tract.
H. L. KRETSCHMER—9. Transurethral resection of the prostate.
F. B. MOOREHEAD—9. Cleft palate surgery; operative treatment of ankylosis of jaw.
DR. GATEWOOD—9. Gastric resection for ulcer.
R. H. HERBST—9. Diverticula of urinary bladder.
R. H. HERBST and C. W. APFELBACH—9. Unusual urinary anomalies.
Staff—9. Dry clinic: E. D. ALLEN, endometriosis; C. P. BAUER, dystocia; AARON KANTER, recognition of early carcinoma of uterus.
G. L. MCWHORTER—10. Fracture of the greater tuberosity of the humerus.
A. VERBRUGGHEN—10. Spinal cord injuries.

Friday

Staff—9. Dry clinic. A. D. BEVAN. Present status of anæsthesia. H. L. KRETSCHMER. Genito-urinary surgery. R. C. BROWN. Treatment of massive hæmorrhage in gastric ulcer. V. C. DAVID. Significance of polyps of large bowel. E. M. MILLER. Method of intravenous injection over long period of time. R. H. HERBST. Fibrosis of bladder neck. F. H. STRAUS. Obstructive jaundice. G. L. MCWHORTER. Reconstruction of common bile duct, cases. M. L. LORING. Granuloma inguinale, cases. S. E. LAWTON. Cholecystenterostomy, indications.
E. J. BERKHEISER—2. Orthopedic clinic.

WASHINGTON BOULEVARD HOSPITAL

Tuesday

PAUL C. FOX—9. Gynecological clinic.

Wednesday

A. R. METZ—9. General surgical clinic, presentation of unusual fractures.

Thursday

V. J. O'CONOR—9. Hydronephrosis, etiology and treatment, case reports, X-rays and operative results; suprapubic prostatectomy and transurethral resection of prostate comparatively, indications and results.

MICHAEL REESE HOSPITAL

Tuesday

ALFRED A. STRAUSS, SIEGFRIED F. STRAUSS, JAMES PATEDJL and ROBERT A. CRAWFORD. Stomach resections for gastric and duodenal ulcer; common duct duodenal anastomosis and gastro-enterostomy for chronic obstructive jaundice.

GEORGE L. DAVENPORT and RALPH BETTMAN. Gall-bladder surgery; surgery of the common duct.

D. C. STRAUSS. Thyroid surgery.

E. FRIEND. General surgery; surgery of the gall bladder.

BERNARD PORTIS. Thyroid surgery; surgery of the rectum.

HARRY RICHTER. Thyroid surgery; gall-bladder surgery.

MAX CUTLER. Surgery of the breast.

GUSTAV KOLISCHER. Diathermy of bladder tumor; nephrectomy for tuberculosis.

IRVING KOLL. Electrical resection of prostate; nephrolithotomy.

DANIEL H. LEVINTHAL. Internal derangements of the knee joint; removal of semi-lunar cartilage; synovectomy for chronic arthritis; bone lengthening operation.

JULIUS E. LACKNER. Abdominal hysterectomy; interposition operation; rectovaginal fistula.

JOSEPH L. BAER and RALPH REIS. Complete perineal laceration, ovarian tumor and pelvic inflammation.

Wednesday

D. C. STRAUSS. Thyroid surgery; gall-bladder surgery.

RALPH BETTMAN. Surgery of the chest.

GEORGE L. DAVENPORT. General surgery.

ALFRED A. STRAUSS, SIEGFRIED F. STRAUSS and ROBERT A. CRAWFORD. Sectional colectomy for ulcerative colitis and pyloroplasty for congenital pyloric stenosis.

BERNARD PORTIS. General surgery and surgery of the colon.

MORRIS L. PARKER. General surgery.

JAMES PATEDJL. General surgery.

JOSEPH EISENSTAEDT. Undescended testis; suprapubic prostatectomy.

HARRY ROLNICK. Electric resection of prostate; pyelotomy for stones.

PHILIP LEWIN and SIDNEY SIDEMAN. Orthopedic clinic, shoulder, elbow, hand, hip, pelvis.

L. E. FRANKENTHAL, SR. and L. E. FRANKENTHAL, JR. Gynecological operations.

W. H. RUBOVITS. Obstetrical and gynecological clinic, demonstration of forceps, version and complete suture, episiotomy.

IRVING STEIN and M. L. LEVENTHAL. Obstetrical clinic, low cervical cæsarean under local anæsthesia.

Thursday

RALPH BETTMAN. Surgery of the gall bladder and common duct.

ALFRED A. STRAUSS, SIEGFRIED F. STRAUSS and ROBERT A. CRAWFORD. Surgical diathermy for carcinoma of the rectum; resections for carcinoma of the stomach.

D. C. STRAUSS. Surgery of the colon, small intestine and thyroid.

GEORGE L. DAVENPORT. Surgery of the common duct.

BERNARD PORTIS. General surgery.

SIEGFRIED F. STRAUSS. General surgery.

HARRY RICHTER. Surgery of the thyroid.

E. FRIEND. Surgery of the gall bladder and common duct.

ALFRED E. JONES. Nephrectomy for tuberculous kidney; suprapubic prostatectomy.

IRVING SHAPIRO. Diathermy of bladder tumor; nephrectomy for tumor of kidney.

DANIEL H. LEVINTHAL. Surgery of the spine, fusion operation for scoliosis and for tuberculosis.

CHARLES M. JACOBS. Orthopedic clinic.

JULIUS E. LACKNER. Gynecological operations.

JOSEPH L. BAER and RALPH REIS. Prolapse; vaginal hysterectomy; fibroids; occiput posterior.

Friday

ALFRED A. STRAUSS, SIEGFRIED F. STRAUSS, JAMES PATEDJL and ROBERT A. CRAWFORD. Subtotal gastrectomy for gastrojejunal ulcer; resection of colon for carcinoma of colon.

D. C. STRAUSS. Surgery of the thyroid and general surgery.

GEORGE L. DAVENPORT and RALPH BETTMAN. Gall-bladder surgery and surgery of the common duct.

RALPH BETTMAN. Thoracic surgery.

BERNARD PORTIS. Surgery of the colon and rectum.

MORRIS L. PARKER. General surgery.

MAX CUTLER. Surgery of the breast; use of radiotherapy in carcinoma.

FREDERICK LIEBERTHAL. Suprapubic prostatectomy; ureterotomy.

J. S. GROVE. Undescended testes.

PHILIP LEWIN and SIDNEY SIDEMAN. Orthopedic clinic, back, hip, knee, foot, shoulder; demonstration of arthritis cases.

L. E. FRANKENTHAL, SR. and L. E. FRANKENTHAL, JR. Gynecological clinic.

W. H. RUBOVITS. Gynecological clinic.

IRVING STEIN and M. L. LEVENTHAL. Gynecological clinic.

WOMEN AND CHILDREN'S HOSPITAL

Monday

FRANCES FORD—2. X-ray therapy in malignancies.

Tuesday

BERTHA VAN HOOSEN—9. General surgical operations.

JOSEPHINE MCCOLLUM and BERTHA VAN HOOSEN—10. Demonstrations of morphine and scopolamine anæsthesia in surgery.

O. ZELEZNY—11. Demonstrations of electrocoagulation therapy.

Wednesday

PEARLE STETLER—9. General surgical operations.

WALBURGA KACIN and CLARA OCHS—2. Obstetrical cases, management under scopolamine anæsthesia.

FRANCES FORD—2. X-ray demonstrations.

PEARLE STETLER—2. Surgical diagnosis of appendicitis in children.

Thursday

ALICE CONKLIN—9. General surgery.

Staff—9. Fracture cases.

MARIE ORTMAYER—10. Urological clinic.

AMELIA GIRYOTAS—11. Carcinoma of the pelvis.

ELOISE PARSONS—2. Endocrine therapy in gynecology; sterility operations.

Friday

MARY E. WILLIAMS—9. Gynecological operations.

CONSTANCE O'BRITIS—11. General surgical operations.

MARY SPIVACK and FLORENCE HARK—2. Obstetrics.

CHARLES FORD—2. X-ray and diathermy therapy.

EVANGELICAL HOSPITAL

G. ERMAN JOHNSON. Clinical studies of extra-uterine pregnancy.

PERCY E. HOPKINS. Clinical studies of pancreatitis.

CHARLES PAPIK. Treatment of lower limb fractures by fixed traction.

PAUL GEORGE PAPSDORF. Demonstration of models and photographs showing newer methods of the handling of fractures of the maxilla and mandible.

MOUNT SINAI HOSPITAL

Tuesday

V. L. SCHRAGER and associates—9. Hernia, breast and biliary surgery.
ISRAEL DAVIDSOHN—11. Pathological demonstration.
M. I. KAPLAN—11. X-ray diagnosis and therapy.
GUSTAV KOLISCHER and HARRY ROLNICK—2. Genito-urinary surgery.

Wednesday

HARRY M. RICHTER and associates—9. Gastric and thyroid surgery.
ISRAEL DAVIDSOHN—11. Pathological demonstration.
M. I. KAPLAN—11. X-ray diagnosis and therapy.
ALFRED A. STRAUSS—2. Gastro-intestinal surgery.
RALPH B. BETTMAN and associates—2. Intrathoracic surgery, operations.

Thursday

AARON KANTER, A. F. LASH and associates—9. Gynecological operations.
ISRAEL DAVIDSOHN—11. Pathological demonstration.
M. I. KAPLAN—11. X-ray diagnosis and therapy.
CHARLES JACOBS and associates—2. Orthopedic operations.

Friday

HARRY ROLNICK—9. Genito-urinary surgery.
ISRAEL DAVIDSOHN—11. Pathological demonstration.
M. I. KAPLAN—11. X-ray diagnosis and therapy.

Dry Clinics—Daily, 9 and 2

ISRAEL DAVIDSOHN. Value of biopsy in surgery.
HENRY BUXBAUM. Toxæmias of pregnancy.
GUSTAV KOLISCHER. Electrosurgery in cancer therapy.
AARON KANTER. Chorio-epithelioma following a vesicular mole; functional uterine hæmorrhage.
HARRY ROLNICK. Bladder tumors.
A. F. LASH. Treatment of birth injury; early diagnosis of uterine cancer.
DAVID A. WILLIS. Relation of adrenals to thyrotoxicosis; morbidity in operation for acute appendicitis in relation to the question of drainage; demonstration of a universal traction splint as used in a small hospital.
EMIL L. AISON. Treatment of fracture of the maxilla and mandible.
M. REESE GUTTMAN. Recent advances in the treatment of malignant diseases about the head and neck; endoscopic clinic.
Staff. Symposium: Cancer of the lung. I. M. TRACE, medical aspect; JACOB LIFSCHUTZ, bronchoscopic aspect; ISRAEL DAVIDSOHN, pathological aspect; M. I. KAPLAN, X-ray aspect.
MAURICE LEWISON. Medical appraisal of surgical risks.

ALBERT MERRITT BILLINGS HOSPITAL

Staff—9, daily. General surgical operations and clinical demonstrations.
WILLIAM ADAMS. Demonstrations in thoracic surgery.
EDMUND ANDREWS. Gall-bladder surgery.
ALEXANDER BRUNSCHWIG. Management of malignant tumors and experimental bone tumors.
E. L. COMPERE, C. H. HATCHER and DR. KEYES. Operations and demonstrations in orthopedic surgery.
LESTER R. DRAGSTEDT. Surgery of the stomach and colon.
C. B. HUGGINS and H. E. HAYMOND. Operations and demonstrations in genito-urinary surgery.
HILGER P. JENKINS. Abdominal surgery.
D. B. PHEMISTER. Bone surgery, operations and demonstrations.

ST. MARY OF NAZARETH HOSPITAL

Monday

A. S. SAMPOLINSKI—2. General surgical clinic.
E. H. WARSZEWSKI and P. F. CZWALINSKI—2. Inguinal hernia clinic.
THAD LARKOWSKI—2. Demonstration of blood transfusion.

Tuesday

GEORGE MUELLER—9. General surgical clinic.
S. R. PIETROWICZ—9. Spinal puncture and anæsthesia—indications, contra-indications, advantages, disadvantages, demonstrations.
C. C. BUCZYNSKI—2. Varicocele operations and demonstrations.
M. J. BADZMIEROWSKI and B. PIERZYNSKI—2. Goiter clinic, operations and demonstration of cases.

Wednesday

T. Z. XELOWSKI—9. Gynecology and abdominal surgery.
W. A. KUFLEWSKI—9. Emergency and general surgery.
THOMAS PLANT—9. General surgery.
A. A. THIEDA—9. General surgery.
FRANK TENZAR—9. General surgery.
JOHN TENZAR—9. General surgery.
CHESTER CHALLENGER—9. X-ray demonstration.
MICHAEL KUTZA—2. General surgery.
F. A. MACKOWIAK—2. General surgery.
M. E. UZNANSKI—2. Obstetrical clinic, low cæsarean section.
M. KRUPINSKI—2. Removal of pilanodal cyst.

Thursday

LEO CZAJA—9. Orthopedic clinic; maggot treatment of osteomyelitis.
E. MACDONALD—9. Abdominal surgery.
H. H. HILL—9. Demonstration of pathological specimens.
A. V. PARTIPILLO—2. Aseptic resection of the bowel, demonstration of cases, moving picture exhibition.
M. E. UZNANSKI—2. Surgical anatomy of the perineum, lantern slide demonstration.

Friday

JOSEPH WELFELD—9. Urological clinic.
GEORGE MUELLER—9. General surgery.
CHESTER CHALLENGER—9. X-ray demonstration.
H. H. HILL—9. Demonstration of pathological specimens.
ROBERT E. FLANNERY—2. Gall-bladder surgery.
LEO P. KOZAKIEWICZ—2. Cæsarean section, indications, contra-indications, demonstrations.

WESLEY MEMORIAL HOSPITAL

Monday

P. B. MAGNUSON—2. Bone surgery.

Tuesday

R. W. MCNEALY—9. Gall-bladder surgery; gastro-intestinal surgery.
C. B. REED—2. Obstetrical clinic, moving picture demonstration of breech delivery, perineorrhaphy and forceps delivery; demonstration of external measurements of intra-uterine child.

Wednesday

PHILIP H. KREUSCHER—9. Joint surgery.
GUY VAN ALSTYNE—9. Osteitis tuberculosa multiplex cystica (Jüngling).

Thursday

G. H. GARDNER and M. T. GOLDSTINE—9. Gynecological clinic, vaginal plastic work.

MERCY HOSPITAL

Tuesday

E. M. BROWN—9. Malignancy of the colon.
J. E. KELLY—9. Chronic intestinal fistula; extensive ventral hernia.
GEORGE GRIFFIN—9. Pyloric obstruction.
J. D. CLARIDGE—9. Fractures and dislocations of the cervical spine.
C. J. LARKIN—9. Rupture of the spleen simulating acute appendicitis.

Wednesday

M. F. MCGUIRE—9. Biliary tract surgery.
C. F. SAWYER—9. Acute pancreatitis; perforating gastric and duodenal ulcers.
C. L. MARTIN—9. Anal fistulectomies in cases with pulmonary tuberculosis.
L. E. GARRISON—9. Carcinoma of the colon; carcinoma of the breast.
HERBERT E. LANDES—9. Surgical anatomy of vesical orifice and urethral obstructions; treatment of bladder tumors.

Thursday

L. D. MOORHEAD—9. Toxic goiters; differential diagnosis of cases of dysthyroidism and hyperthyroidism with indication for operation and management.
W. J. PICKETT—9. Technical considerations in posterior gastro-enterostomy.
F. E. PIERCE—9. Fracture cases.
F. M. DRENNAN and F. C. VALDEZ—9. Gastro-intestinal clinic.

Friday

HENRY SCHMITZ and HERBERT E. SCHMITZ—9. Gynecological clinic; surgery and radiation therapy.
JOSEPH LAIBE—9. Carcinoma of the genito-urinary tract.
A. M. VAUGHN—9. Cystic hygroma in an infant.

FRANCES E. WILLARD HOSPITAL

Tuesday

ALLEN E. STEWART—9. General surgical clinic.
FREDERICK MUELLER—3. Surgery of bones and joints.

Wednesday

OTIS M. WALTER—9. General surgical clinic.
VAUGHN L. SHEETS—10. Diabetic clinic.

Thursday

JOSEPH F. JAROS—9. Thyroid clinic.

Friday

VICTOR L. SCHRAGER—9. General surgical clinic.

EVANGELICAL DEACONESS HOSPITAL

Tuesday

EDWARD HEACOCK—9. General surgery.

Wednesday

PAUL MORF—9. General surgery.

Thursday

A. J. SCHOENBERG—9. Pelvic surgery.

Friday

JOHN PEARL—9. Abdominal surgery; spinal anæsthesia.

RAVENSWOOD HOSPITAL

Tuesday

G. W. GREEN—9. Gall-bladder surgery, mortality and morbidity.
C. A. BUSWELL—9:30. Survey of cancer study organization in a private hospital.
D. B. POND—10. Orthopedic surgery.
E. W. MUELLER and J. J. MOORE—10:30. Carcinoma of testis.
M. FIELD—11. Diagnosis and management of sterility.
L. C. FRENCH and D. L. JENKINSON—11:30. Gastric syphilis.

Wednesday

G. DE TARNOWSKY and J. J. MOORE—9. Carcinoma of colon, modified Kraske operation.
J. IRELAND—9:30. Fractures of the elbow.
R. F. WEISSBRENNER—10. Emotions as etiological factors in hyperthyroidism.
C. H. LOCKWOOD—10:15. Headaches.
H. P. SAUNDERS—11. Blood transfusion.
L. E. DAY—11:15. Obstetrics.
J. F. OATES—11:30. Spinal anæsthesia.

Thursday

C. C. RENTFRO—9. Obstetrical anæsthesia.
W. F. GROSVENOR—9:15. Cæsarean section.
A. C. HAMMETT—9:30. Mental disturbances of diabetic patients.
A. V. BERGQUIST—9:45. Indigestion.
F. N. BUSSEY—10. Granulosa cell carcinoma of ovary.
R. E. DYER—10:30. Surgical technique.
P. J. SARMA—11. Paramedian abdominal incision.
F. R. VON NAHOWSKI—11:15. Mortality in appendicitis.
E. B. WILLIAMS—11:30. Perthes' disease; fracture of spine.

SHRINERS' HOSPITAL

Tuesday

BEVERIDGE MOORE and HAROLD SOFIELD—9. Orthopedic operations.

Wednesday

BEVERIDGE MOORE—2. Demonstration of plaster technique; club foot clinic.

Thursday

BEVERIDGE MOORE and HAROLD SOFIELD—9. Orthopedic operations.

Friday

BEVERIDGE MOORE and HAROLD SOFIELD—2. Out-patient clinic.

SOUTH CHICAGO COMMUNITY HOSPITAL

Tuesday

M. E. FINSKY—2. Avertin anæsthesia, analysis of 200 cases.
LOUIS D. SMITH—2:30. Tuberculosis of the kidney, presentation of case.

Friday

JOSEPH J. LEBOWITZ—2. Fractures and dislocations of the elbow, presentation of cases treated by open operation.
FRANK G. MURPHY—2:30. Fractures of the upper end of the humerus, presentation of cases.
GEORGE G. O'BRIEN—3. Postoperative evisceration, presentation of case.

JACKSON PARK HOSPITAL

Monday

F. L. BARBOUR—2. Dry clinic: Symposium on treatment of pulmonary tuberculosis, surgical and medical.

Tuesday

T. H. KELLEY—9. General surgical clinic.
ARRIE BAMBERGER—10. General surgical clinic.
C. C. CLARK—11. General surgical clinic.
S. B. MACLEOD—2. Fracture clinic.

Wednesday

ARRIE BAMBERGER—9. General surgical clinic.
H. HOYT COX—10. General surgical clinic.
S. W. MARCHMONT-ROBINSON—2. Dry clinic: Hand infections as related to industrial surgery.
H. F. SPIERLING—3. Mortality of appendicitis.

Thursday

ARRIE BAMBERGER—9. General surgical clinic.
T. H. KELLEY—10. General surgical clinic.
G. MARCHMONT-ROBINSON—11. Injection treatment of hæmorrhoids.
E. ALLEN PARSONS—12. Postoperative treatment of ruptured appendix with peritonitis.
R. T. FARLEY—1. Chorio-epithelioma; pseudo Addison's disease; volvulus.
J. J. MOORE—2. Gross surgical pathology.

Friday

A. F. HENNING—9. General surgical clinic.
GEORGE M. LUCAS—10. Gynecological surgery.
C. C. CLARK—11. General surgical clinic.

HOSPITAL OF ST. ANTHONY DE PADUA

Monday

THOMAS DWYER—2. Demonstrations in surgical pathology.

Tuesday

LAWRENCE RYAN—9. General surgery.
J. J. SPRAFKA—9. General surgery.
O. J. JIRSA—9. Urology.
L. S. TICHY—2. X-ray demonstration.

Wednesday

R. C. CUPLER—9. General surgery.
JOSEPH ZABOKRTSKY—9. General surgery.
F. W. SLOBE—2. Fracture clinic.
M. A. WEISSKOPF—2. Obstetrics.

Thursday

FRANK J. JIRKA—9. Abdominal operations.
F. B. OLENTINE and R. C. DRURY—9. Thyroid surgery and general surgical clinic.
O. J. JIRSA—9. Urology.
L. S. TICHY—2. X-ray demonstration.

Friday

S. E. DONLON—9. General surgery.
A. A. BONA—9. General surgery.
M. A. WEISSKOPF—9. Obstetrics.

HENROTIN HOSPITAL

Tuesday

CHANNING BARRETT—9. Gynecological operations.
F. LEE STONE—9. Some problems in tubal patency.

Wednesday

JOHN A. GRAHAM—11. Open reduction of fractures.

COLUMBUS HOSPITAL

Tuesday

DANIEL A. ORTH, C. O. LINDSTROM and M. L. HANNAN—9. General surgery.
DANIEL A. ORTH—9. Indications and contra-indications for spinal anæsthesia.
CHANNING BARRETT—9. Gynecological operations.
MINAS JOANNIDES—9. Collapse therapy in pulmonary tuberculosis.
M. J. SEIFERT—10. Surgical treatment of ulcer of the stomach.
MINAS JOANNIDES—2. Surgery of the chest.

Wednesday

CHANNING BARRETT—9. Gynecological clinic.
G. N. BEECHER and M. B. BURNS—9. Emergency surgery in industrial injuries.

Thursday

MINAS JOANNIDES—9. Surgical treatment of abscess of lung.
F. MUELLER and F. MUELLER, JR.—9. Transplantation of bone.
WILLIAM GEHL and T. L. CHENOWETH—9. Urological clinic.
G. N. BEECHER and M. B. BURNS—9. Emergency surgery in industrial injuries.

Friday

DANIEL A. ORTH, C. O. LINDSTROM and M. L. HANNAN—9. General surgery.
M. J. SEIFERT—9. General surgery.

MUNICIPAL TUBERCULOSIS SANITARIUM

Tuesday

CLEMENT L. MARTIN—9. Perianal tuberculosis.
MINAS JOANNIDES—9. Thoracoplasty; phrenic neurectomy.
HENRY C. SWEANY—11. Pathological conference, demonstration of pathological specimens.

Wednesday

DORRIN F. RUDNICK—9. Nephrectomy for tuberculosis of kidney; operative surgery for tuberculosis of the genito-urinary tract.
FRANK FREMMEL and FRANK SMEJKAL—10. Artificial pneumothorax.
FREDERICK TICE, ALLAN J. HRUBY and K. J. HENRICHSEN—2. Diagnostic clinic.

Thursday

JEROME HEAD and RICHARD DAVISON—9. Thoracoplasty; pneumolysis; phrenic neurectomy.
K. J. HENRICHSEN—9. Artificial pneumothorax.

Friday

JEROME HEAD and K. J. HENRICHSEN—9. Surgical conference.

OUTPATIENT PNEUMOTHORAX CLINIC

2049 Washington Boulevard

MINAS JOANNIDES, E. L. QUINN, EMIL BUNTA and CLARA JACOBSON—9 and 2, daily. Artificial pneumothorax on ambulatory patients.

ALEXIAN BROTHERS HOSPITAL

Tuesday

MALCOLM L. HARRIS, AUGUST ZIMMERMAN, ROBERT FLANNERY and GEORGE L. APFELBACH—9. General surgery.
A. WOCHINSKI and EDWARD WHITE—9. General surgery.

CHICAGO MEMORIAL HOSPITAL

Monday

JULIA C. STRAWN and PAUL M. CLIVER—9. Gynecological clinic.

Tuesday

ARTHUR H. CONLEY and FRED M. MILLER—9. Orthopedic and industrial injury clinic.
JAMES E. FITZGERALD—2. Obstetrical clinic.
JOHN P. O'NEIL, J. WILLIAM PARKER and DORRIN F. RUDNICK—2. Urological clinic.

Wednesday

CHARLES E. KAHLKE, LAWRENCE L. ISEMAN, ROBERT A. MELENDY and M. L. WEINSTEIN—9. General surgical clinic.
FRANK WRIGHT—9. Colloidal state of the blood in postoperative pneumonia.
GEORGE M. LANDAU—2. Phrenico exeresis and treatment of unilateral tuberculosis.

Thursday

C. R. G. FORRESTER—9. Fracture clinic.
CASPER M. EPSTEIN—9. Oral and plastic surgery.
CHARLES J. DRUECK, SR.—2. Proctology.
HARRY L. MEYERS—2. Gynecological clinic.
WILLIAM L. BROWN—2. Radium clinic.

Friday

PETER S. CLARK, BENNETT R. PARKER and LEO M. ZIMMERMAN—9. General surgical clinic.

ILLINOIS MASONIC HOSPITAL

Tuesday

E. WHITE—9. Prostatic surgery.
O. C. RITCH—9. Surgery of the kidney.
CLARENCE SAELHOF—9. Tumors of the testicle.

Wednesday

GILBERT FITZPATRICK—9. Obstetrical problems.
CHARLES PARKES and J. R. HARRY—9. Gall-bladder problems.
CARL F. STEINHOFF—9. Medical consideration of thyroid disease.
HUGH MACKECHNIE—9. Surgery of the thyroid.

Thursday

C. K TIMMONS—9. Surgical considerations of peptic ulcer.
J. F. DAVIS—9. Surgery of the colon.
WALTER FISCHER—9. Orthopedic problems of the feet.

ILLINOIS CENTRAL HOSPITAL

Tuesday

HUGH M. MACKECHNIE—9. General surgery.
PHILIP H. KREUSCHER—9. Orthopedics.

Wednesday

CHARLES PFEIFFER—9. General surgery.
BEVERIDGE MOORE—9. Orthopedics.

Thursday

S. CLEMENT HOGAN—9. General surgery.
VICTOR LESPINASSE—9. Genito-urinary surgery.

Friday

WILLIAM T. HARSHA—9. General surgery.
JAMES GILL—9. Neurologic surgery.
JOHN J. HILL—9. Obstetrics.
CHESTER GUY and A. H. BAUGHER—9. Pathological conference.

AUGUSTANA HOSPITAL

Tuesday

N. M. PERCY and O. E. NADEAU—9. Goiter and general surgical clinic.

Wednesday

A. T. LUNDGREN and EARL GARSIDE—9. General surgical clinic.
J. W. NUZUM—9. General surgical clinic.
R. J. ODEN—9. General surgical clinic.

Thursday

N. M. PERCY and O. E. NADEAU—9. Goiter and general surgical clinic.

Friday

A. T. LUNDGREN and EARL GARSIDE—9. General surgical clinic.
J. W. NUZUM—9. General surgical clinic.
R. J. ODEN—9. General surgical clinic.

AMERICAN HOSPITAL

Tuesday

R. B. MALCOLM—9. Surgical clinic, tumors of the neck.
MAX THOREK and PHILIP THOREK—9. Surgical clinic, carcinoma of the rectum.
W. B. GERHARD—9. General surgical clinic.
FRANK E. SIMPSON—2. Radium treatment of carcinoma of the mouth and tongue.
SOLOMON GREENSPAHN and FREDERICK BOWE—2. Management of placenta prævia.

Wednesday

MAX THOREK and PHILIP THOREK—9. Surgery of the biliary tract.
HORACE E. TURNER and S. GREENSPAHN—9. Casualty surgical clinic.
L. W. BREMERMAN, DAVIS H. PARDOLL and LEON BEILIN—9. Urological clinic.
FRANK E. SIMPSON—2. Radiological clinic, carcinoma of the breast and female genitalia.

Thursday

BENJAMIN GOLDBERG and JOHN F. PICK—9. Indications and technique for surgery of the chest.
FRANK E. SIMPSON—2. Radiological clinic, indications and contra-indications to radium treatment.

CHILDREN'S MEMORIAL HOSPITAL

Monday

FREMONT A. CHANDLER, CHARLES N. PEASE and FERDINAND SEIDLER—2. Orthopedic clinic.

Tuesday

FREMONT A. CHANDLER, FERDINAND SEIDLER and CHARLES PEASE—9. Orthopedic operations.
FREDERICK B. MOOREHEAD—2. Oral surgery, operations and demonstration of cases.

Wednesday

ALBERT H. MONTGOMERY and staff—9. General surgery, operations and demonstration of cases.

Thursday

HERMAN L. KRETSCHMER and staff—9. Urological surgery, operations and demonstration of cases.

Friday

ALBERT H. MONTGOMERY and staff—9. General surgery, operations and demonstration of cases.

CHICAGO LYING-IN HOSPITAL

Staff: FRED L. ADAIR, J. B. DELEE, WILLIAM J. DIECKMANN, M. EDWARD DAVIS, FRANK E. WHITACRE, MANUEL SPIEGEL and H. C. HESSELTINE.

Monday

Staff—2. Obstetrical operations, motion picture demonstration.

Tuesday

Staff—9. Obstetrical and gynecological operations.

Wednesday

Staff—9. Obstetrical and gynecological operations.
Staff—2. Obstetrical clinic, motion picture demonstration.

Thursday

Staff—9. Obstetrical and gynecological operations.
Staff—2. Obstetrical and gynecological dry clinic, motion picture demonstration.

Friday

Staff—9. Obstetrical and gynecological operations.
Staff—2. Obstetrical and gynecological dry clinic, motion picture demonstration.

RESEARCH AND EDUCATIONAL HOSPITAL

Monday

H. B. THOMAS—1. Orthopedic surgery.

Tuesday

CARL A. HEDBLOM and WILLARD VAN HAZEL—9. Thoracic and general surgery.
L. S. SCHULTZ—9. Oral surgery.

Wednesday

ERIC OLDBERG—9. Neurological surgery.
R. B. MALCOLM—9. General surgery.
H. B. THOMAS—1. Orthopedic surgery.
F. H. FALLS—2. Obstetrical and gynecological clinic.

Thursday

CHARLES B. PUESTOW—9. General surgery.
C. M. MCKENNA—10. Urological clinic; cystoscopies.
WILLARD VAN HAZEL—2. Thoracic surgery.

Friday

CARL A. HEDBLOM and WILLARD VAN HAZEL—9. Thoracic and general surgery.
F. H. FALLS—2. Obstetrical and gynecological clinic.

POST-GRADUATE HOSPITAL

Monday

B. C. CUSHWAY—2. X-ray diagnosis.

Tuesday

H. SOLOWAY—10. Urological clinic.
EMIL RIES—10. Gynecological operations.
D. SCHLAPIK—2. Intraurethral prostatectomy, moving picture demonstration.

Wednesday

J. C. BOODEL—10. Rectal operations
LEO ZIMMERMAN—2. Phlebitis

Thursday

H. L. MEYERS—10. Gynecological operations.
R. A. LIFVENDAHL—11. Gynecological clinic with colposcopic demonstration.

Friday

EMIL RIES—10. Gynecological operations.

SOUTH SHORE HOSPITAL

Tuesday

AXEL WERELIUS—9. Gastric surgery.
GEORGE G. O'BRIEN—11. General surgery.
CLARENCE S. DUNER and AXEL WERELIUS—2. Symposium on gastric and duodenal ulcer.

Wednesday

HUGH MACKECHNIE—9. Surgery of the colon.
FRANK G. MURPHY—11. Orthopedic clinic.
H. WILLIAM ELGHAMMER, GUY S. VAN ALSTYNE and PAUL R. CANNON—2. Symposium on intussusception.

Thursday

LOUIS D. SMITH—9. Genito-urinary surgery.
CLARA JACOBSON—2. Lung collapse procedures.
C. C. MAHER—3. Cardiac risk in surgery.

Friday

E. A. LUTTON—9. Gynecological clinic.
ANDREW DAHLBERG and WILLIAM HANRAHAN—11. Operative obstetrics.
H. R. COLVER—2. Industrial surgery.
WALTER FISCHER—3. Foot problems.

JOHN B. MURPHY HOSPITAL

Monday

JOSEPH KEREKES and R. J. MURPHY—2. Rectal treatment of appendiceal and other pelvic abscesses.

Tuesday

H. E. DAVIS—10. Studies of epiphyseal growth disturbances.

Wednesday

M. J. PURCELL—10. Emergency surgery.
O. H. SCHULZ—10. Observations on treatment of pneumonia.

Thursday

F. O. BOWE—9. Treatment of puerperal infections.
H. R. KENNEY and S. J. MARK—10. General surgery.

Friday

A. C. GARVY—10. Diagnosis and treatment of skull fractures.
H. R. KENNY and S. J. MARK—10. Pre-operative treatment in abdominal cases.

GRANT HOSPITAL

Tuesday

ANDRE L. STAPLER—9. General surgery.
F. H. FALLS—9. Gynecology.
E. FISCHMANN—9. Vaginal hysterectomy.
A. G. FREY—9. General surgery.
GEORGE ABELIO—9. General surgery.
E. HESS—10. Urology.

Wednesday

E. SEIDLER—9. Midtarsal resection.
A. G. ZIMMERMAN—9. General surgery.

Thursday

B. H. ORNDOFF—9. Electrosurgery.
W. A. STUHR—9. General surgery.
ANDRE L. STAPLER—2. General surgery.

Friday

SYLVAN COOMBS—9. General surgery.
E. W. FISCHMANN—9. Pus tubes.
A. G. ZIMMERMAN—9. General surgery.

ST. JOSEPH HOSPITAL

Monday

HUGH MCKENNA—2. Review of traumatic surgery with special reference to fractures.

Tuesday

FRANKLIN B. MCCARTY—9. Surgical anatomy, pathology and surgical treatment of diseases of the gall bladder.
RALPH A. KORDENAT—2. Breast tumors.

Wednesday

HUGH MCKENNA—9. Abdominal surgery, surgery of the large intestine.
WALTER W. VOIGT—9. Puerperal sepsis.
THOMAS J. O'DONOGHUE—2. Obstetrical and gynecological operations.

Thursday

WILLIAM H. G. LOGAN—9. Cleft palate and cleft lip operations.
RALPH A. KORDENAT—2. Gall-bladder surgery.

Friday

L. WADE MARTIN—9. Obstetrical clinic.

OAK PARK HOSPITAL

Tuesday

JOHN W. TOPE—9. General surgery.
GORDON SWANSON—9. Orthopedic clinic.
ARTHUR CONLEY—9. Management of fractures of the femur.

Wednesday

RALPH SULLIVAN—9. General surgical clinic, treatment of peptic ulcer.
CHARLES FOX—9. Gynecological operations.
CARL UTHOFF—9. Operative cystoscopy.

Thursday

LOUIS RIVER—9. General surgery.
ADOLPH KRAFT—9. General surgery.
CARL UTHOFF—9. Genito-urinary operations.

Friday

JOHN W. TOPE—9. General surgery.
MEREDITH MURRAY—9. Gynecological operations.

WEST SUBURBAN HOSPITAL

Monday

HARRY J. DOOLEY—2. Urological clinic.

Tuesday

WILLIAM J. POTTS—9. The healing of fractures.
OSCAR B. FUNKHOUSER—9. Gall-bladder surgery.
THOMAS I. MOTTER—9. General surgery.
JAMES H. SKILES—9. Gynecological clinic.

Wednesday

JOSEPH L. NORTELL—9. General surgery.
FREDERICK H. FALLS—9. Gynecological clinic.

Thursday

CHARLES E. HUMISTON—9. General surgery.
WARD E. POTTER—9. Thyroid clinic.
LOUIS FAULKNER—9. Interesting obstetrical conditions.
PAUL C. FOX—9. Gynecological clinic.
EUGENE C. PIETTE—9. Pathological demonstration.
HOMER HUMISTON—2. Urological clinic.

ST. ANNE'S HOSPITAL

Tuesday

T. E. MEANY—10. Orthopedic clinic.
J. L. KNAPP—11. General surgery.
J. B. HARNEY—2. X-ray demonstration.

Wednesday

G. F. THOMPSON—9. Stomach and intestinal surgery.
J. W. MCCONNELL—10. Gynecology.
J. J. GEARIN—11. General surgery.

Thursday

H. J. DOOLEY—9. Urological clinic.
E. P. VAUGHAN—9. Gall-bladder surgery.
E. P. GRAMER—10. Treatment of head injuries.
J. L. FLEMING—11. Pathological obstetrics.

Friday

B. W. MACK—9. General surgery.
Staff—10. Clinical meeting.
D. F. HAYES—11. General surgery.
L. R. HILL—2. Pathological demonstration.

HOLY CROSS HOSPITAL

Tuesday

J FRANCIS RUZIC—9. Gynecological operations; cholecystectomy, high spinal anæsthesia.
E. R. CROWDER—9. Some practical considerations regarding the Graham test.
JOHN F. DYBALSKI—10. Hysterectomy, spinal anæsthesia.
VINCENT TORCZYNSKI—11. Appendectomy.

Wednesday

DONALD MONACO—9. Thyroidectomy; lecture on avertin anæsthesia.
A. R. MCCRADIE—10. Hernia operation.
PAUL LAWLER—11. Low cervical cæsarean section.

Thursday

STEPHEN BIEZIS—9. Gynecological operations.
MICHAEL STRIKOL—10. Cholecystectomy.
F. F. FRAIDER—11. Panhysterectomy.

Friday

M. J. BADZMIEROWSKI—9. Thyroidectomy; hysterectomy.
RICHARD ROCHE—10. Herniorrhaphy.
J. FRANCIS RUZIC—11. Pre- and postoperative therapy.

GARFIELD PARK HOSPITAL

Tuesday

JOHN R. HARGER and SAM PLICE—9. Surgery of the stomach; treatment of peptic ulcer.
L. F. MACDIARMID—9. General surgery.

Wednesday

CLAUDE WELDY and JOHN H. PFLOCK—9. Abdominal surgery.

Thursday

J. M. BERGER and FRANK CHAUVET—9. General surgery.

Friday

CLARENCE SAELHOF—9. Dipliasic strains of bacteria from renal lesions; experimental production of lesions with spironenia (spirochæta Pallida).
VINCENT J. O'CONOR—9. Tuberculosis of kidney with review of cases; hydronephrosis, plastic repair of nephropexy.

EVANSTON HOSPITAL

Monday

JAMES T. CASE—2. X-ray diagnosis and therapy.

Tuesday

WILLIAM R. PARKES—9. Thyroid clinic.
MARCUS H. HOBART—9. General surgical clinic.
DWIGHT F. CLARK—2. Recent advances in the treatment of common fractures.
MARCUS H. HOBART—2. Fracture clinic.

Wednesday

WILLIAM C. DANFORTH—9. Gynecological operations.
CHARLES E. GALLOWAY—9. Gynecological operations.
JEROME R. HEAD—9. Thoracic surgery.
FREDERICK CHRISTOPHER—2. Demonstration of surgical cases.
ROBERT C. LONERGAN—2. Demonstration of orthopedic cases.

Thursday

WILLIAM C. DANFORTH—9. Gynecological operations.
JOHN L. PORTER—9. Orthopedic operations.
WILLIAM C. DANFORTH—2. Obstetrical clinic.
CHARLES E. GALLOWAY—2. Schiller test for the early diagnosis of carcinoma of the cervix.

Friday

FREDERICK CHRISTOPHER—9. General surgical clinic.
FRANCIS D. GUNN—9. Demonstration of surgical pathology.
CHARLES E. POPE—9. Proctological clinic.
J. EVERETT SANNER—2. Urological clinic.

LUTHERAN DEACONESS HOSPITAL

Tuesday

GEORGE H. SCHROEDER, JOHN KOUCKY, H. C. WALLACE and G. H. MAMMEN—9. General surgical clinic.

Wednesday

GEORGE H. SCHROEDER, JOHN KOUCKY, H. C. WALLACE, G. H. MAMMEN, R. G. WILLY and G. O. SOLEM—9. Clinical demonstrations.

Thursday

GEORGE H. SCHROEDER, JOHN KOUCKY, H. C. WALLACE and G. H. MAMMEN—9. General surgical clinic.

Friday

GEORGE H. SCHROEDER, JOHN KOUCKY, H. C. WALLACE, G. H. MAMMEN, R. G. WILLY and G. O. SOLEM—9. Clinical demonstrations.

ST. BERNARD'S HOSPITAL

Monday

W. G. EPSTEIN—2. General surgery.

Tuesday

W. J. MULHOLLAND—9. General surgery.
H. HOFMANN—9. General surgery.
G. M. CUSHING—2. General surgery.
L. B. DONKLE—2. Genito-urinary surgery.

Wednesday

B. C. CUSHWAY and R. J. MAIER—9. Roentgenological demonstration of anomalies of spine.
J. B. HAEBERLIN—9. General surgery.
W. S. HECTOR—9. General surgery.
J. A. PARKER—2. General surgery.
S. L. GOVERNALE and S. S. MARKIEWICZ—2. Gastro-intestinal operations.

Thursday

J. T. MEYER—9. Thyroid surgery.
F. M. PHIFER—9. Genito-urinary surgery.
W. P. GUNN—9. Gynecological operations.
D. A. VLOEDMAN—2. Gynecological operations.
C. C. GUY—2. Demonstration of unusual specimens.

Friday

A. E. MCCRADIE—9. General surgery.
E. A. RACH and F. J. STUCKER—9. Operative obstetrical problems.

LITTLE COMPANY OF MARY HOSPITAL

Monday

W. D. STADLE—2. Management of eclamptic patients.

Tuesday

L. L. CHARPIER—9. Management of fractures about the elbow.
J. E. LAIBE—10. Treatment of carcinoma of the bladder.

Wednesday

E. D. HUNTINGTON—9. Gastro-intestinal surgery, complications.

Thursday

L. L. CHARPIER—9. Management of compound fractures.
W. A. MALONE—10. Radium treatment of carcinoma of the cervix.

Friday

A. W. WOODS—9. Gynecological repair operations.
E. D. HUNTINGTON—10. Intestinal obstruction.

SURGERY OF THE EYE, EAR, NOSE AND THROAT

RESEARCH AND EDUCATIONAL HOSPITAL

Otolaryngological Staff: F. L. Lederer, W. H. Theobald, J. J. Theobald, G. S. Livingston, E. A. Bredlau, N. Fox, S. L. Shapiro, I. G. Spiesman, P. A. Halper, A. C. Kane, A. Coombs, J. Harned, O. Van Alyea, M. Guttman, S. Morwitz, M. Ostrom, B. Lambrakis, E. Hartlett, H. Klawans, L. Fishman, H. Wadsworth, J. Bellows and N. Fabricant.

Ophthalmological Staff: Hallard Beard, M. L. Folk, H. J. Smith, S. Wolf, S. Kaufman, Carl Apple and J. W. Clark.

Monday

Staff—2. Otolaryngological out-patient clinic.

Tuesday

Staff—9. Ophthalmological clinic, operations and demonstrations.
Staff—10. Otolaryngological out-patient clinic.
Staff—2. Otolaryngological clinic, operations and demonstrations.

Wednesday

Staff—9. Eye clinic.
Staff—10. Otolaryngological out-patient clinic.
Staff—2. Otolaryngological out-patient clinic.
Staff—4. Otolaryngological seminar.

Thursday

Staff—9. Otolaryngological operations.
Staff—9. Eye clinic.
Staff—10. Otolaryngological out-patient clinic.
Staff—2. Otolaryngological clinic, operations and demonstrations.
Staff—2. Otolaryngological out-patient clinic.

Friday

Staff—9. Eye clinic, operations and demonstrations.
Staff—10. Otolaryngological out-patient clinic.
Staff—2. Otolaryngological out-patient clinic.

MERCY HOSPITAL

Tuesday

George T. Jordan—9. Nasal ganglion.
L. G. Hoffman—9. Cataract extractions.
C. H. Christoph—9. Bronchoscopy.

Wednesday

George Musgrave and Alfred Paisley—9. Frontal sinus operation, local anæsthesia; modified radical mastoid operation with complete removal of flap; presentation of cases.

Thursday

Ulysses J. Grim—9. Radical antrum and mastoid.
Deno O'Connor and Ray Kerwin—9. Ocular tumors.
Carl Schaub—9. Focal infection in iritis.

EVANSTON HOSPITAL

Tuesday

Thomas C. Galloway—9. Otolaryngological clinic.

Thursday

Howard C. Ballenger—9. Otolaryngological clinic.

Friday

Gail R. Soper—2. Lesions of the fundus oculi, lantern slide demonstration.

PRESBYTERIAN HOSPITAL AND RUSH MEDICAL COLLEGE

Monday

D. B. Hayden—2. Complications of otitis media without rupture of the tympanic membrane.
E. W. Hagens—2. Unusual laryngeal and bronchial case.
George E. Shambaugh, Jr. and E. W. Hagens—2. Operations on the tear sac for dacrocystitis.
Max Jacobson—3. Neurological aspects.

Tuesday

Robert von der Heydt—3. Slit lamp diagnostic clinic.

Wednesday

Vernon Leech—3. Glaucoma.

Thursday

Bertha Klein—10. Histopathology of fundus.
T. W. Lewis—2. Discussion of some difficult problems in the operation for correction of the nasal septum.
L. T. Curry—2. Demonstration of skiagraphs of the sinuses and mastoids.
R. W. Watkins—2. Nasal findings in allergic cases.
W. J. Jonker—2. Diathermy and its application to the treatment of nose and throat conditions.

Friday

W. F. Moncreiff—10. External diseases of the eye and iridocyclitis.
Elias Selinger—3. Fundus.

ILLINOIS EYE AND EAR INFIRMARY

Tuesday

Dwight C. Orcutt—9. Use of flap in cataract work; superior rectus tension suture; plastic.
LeRoy Thompson—9. Industrial ophthalmology.
Carl H. Christoph—10. Bronchoscopy; œsophagoscopy.
M. A. Glatt—1. Radical mastoid and radical frontal operations.
Oscar Cleff—3. Radical mastoid operation.
E. R. Crossley—2. Intra- and extra-ocular surgery.

Wednesday

M. Lebensohn—9. Detachment of retina; cataracts; trephine.
Staff—10. Dry clinic.
Ulysses J. Grim—1. Radical mastoid and radical antrum operations.
Michael Goldenburg—2. Iridotasis operation for glaucoma; cataracts; controlled tenotomy.
John A. Cavanaugh—3. Radical mastoid operation.

Thursday

Herbert Walker—9. Detachment of retina, Larson operation.
C. F. Yerger—10. Radical sinus and radical mastoid operations.
A. Lewy—1. Radical frontal operation.
E. K. Findlay—2. Intra- and extra-ocular surgery.
W. A. Gross—3. Tonsils, diathermy.

RAVENSWOOD HOSPITAL

Wednesday

A. N. Murray—10:30. Malignancies of the eye.

CHICAGO EYE, EAR, NOSE AND THROAT HOSPITAL

Tuesday

H. B. FULLER—9. Mastoid surgery.
WILLIAM A. HOFFMAN and WILLIAM LINGARD—9. Ear, nose and throat clinic.
WILLIAM A. FISHER—9. Cataract operations.
WILLIAM A. HOFFMAN—9. Eye clinic.
L. SAVITT—10. Removal of tonsils by diathermy.
OSCAR B. NUGENT—11. Eye clinic.
O. M. STEFFENSON—11. Ear, nose and throat clinic.
T. S. KAMMERLING—2. Eye, ear, nose and throat clinic.

Wednesday

O. M. STEFFENSON—9. Tonsil dissection.
WILLIAM A. HOFFMAN and WILLIAM LINGARD—9. Nasal surgery and ear, nose and throat clinic.
OSCAR B. NUGENT—9. Cataract operations.
WILLIAM A. HOFFMAN—9. Eye clinic.
OSCAR B. NUGENT—11. Eye clinic.
O. M. STEFFENSON—11. Ear, nose and throat clinic.
L. SAVITT—11. Ear, nose and throat clinic.
H. B. FULLER—2. Eye, ear, nose and throat clinic.

Thursday

WILLIAM A. FISHER—9. Eye operations.
WILLIAM A. HOFFMAN—9. Eye clinic.
T. S. KAMMERLING—9. Surgery of the nasal accessory sinuses.
WILLIAM A. HOFFMAN and WILLIAM LINGARD—9. Ear, nose and throat clinic.
L. SAVITT—10. Physical measures in otolaryngology.
O. M. STEFFENSON—11. Ear, nose and throat clinic.
L. SAVITT—11. Ear, nose and throat clinic.
OSCAR B. NUGENT—11. Eye clinic.
T. S. KAMMERLING—2. Eye, ear, nose and throat clinic.

Friday

O. M. STEFFENSON—9. Tonsil dissection.
WILLIAM A. HOFFMAN and WILLIAM LINGARD—9. Ear, nose and throat clinic.
OSCAR B. NUGENT—9. Fundus photography and pathology.
WILLIAM A. HOFFMAN—9. Eye clinic.
H. B. FULLER—10. Functional testing.
O. M. STEFFENSON—11. Ear, nose and throat clinic.
OSCAR B. NUGENT—11. Eye clinic.
H. B. FULLER—2. Eye, ear, nose and throat clinic.

MICHAEL REESE HOSPITAL

Monday

H. S. GRADLE—2:30. Eye surgery.

Tuesday

S. J. PEARLMAN—9. Bronschoscopic clinic.
M. L. FOLK—2. Eye surgery.

Wednesday

SAMUEL SALINGER—9. Nasal fractures; plastic of the nose.
M. L. FOLK—2. Eye clinic.
H. S. GRADLE—2:30. Surgical eye clinic.
ROBERT VON DER HEYDT—3. Slit-lamp demonstration.

Thursday

CASPER EPSTEIN—9. Cleft palate and harelip.
S. J. MEYER—2. Eye clinic.

ALBERT MERRITT BILLINGS HOSPITAL

Tuesday

E. V. L. BROWN—9. Eye clinic.
J. R. LINDSAY—10:30. Ear, nose and throat clinic.
DEWEY KATZ—2. Eye clinic.

Wednesday

LOUIS BOTHMAN—9. Eye clinic.
T. E. WALSH—10:30. Ear, nose and throat clinic.
JOHN STOUGH—2. Eye clinic.
J. R. LINDSAY and G. H. SCOTT—2. Ear, nose and throat operations.

Thursday

P. C. KRONFELD—9. Eye clinic.
G. H. SCOTT and H. B. PERLMAN—10:30. Ear, nose and throat clinic.
DEWEY KATZ—2. Eye clinic.

Friday

DEWEY KATZ—9. Eye clinic.
J. R. LINDSAY and T. E. WALSH—10:30. Ear, nose and throat clinic.
P. C. KRONFELD—2. Eye clinic.
T. E. WALSH and H. B. PERLMAN—2. Ear, nose and throat operations.

COOK COUNTY HOSPITAL

Monday

EARLE B. FOWLER—2. Ophthalmoscopy.
S. PEARLMAN and N. LESHIN—2. Œsophagoscopy and bronchoscopy; surgery of the neck.

Tuesday

THOMAS D. ALLEN—2. External diseases of the eye.
I. MUSKAT—2. Clinical and surgical otolaryngology; plastic surgery of face and nose.

Wednesday

L. T. CURRY—9. Otolaryngology, clinical and surgical cases.
WILLIAM F. MONCREIFF—9. Ophthalmic neurology and ophthalmoscopy.

Thursday

SANFORD R. GIFFORD—9. Ophthalmic surgery.
CHARLES F. YERGER—11. External diseases of the eye.
S. PEARLMAN and N. LESHIN—2. Œsophagoscopy and bronchoscopy; surgery of the neck.

Friday

T. C. GALLOWAY and M. T. LAMPERT—10. Malignancy about the head, diathermy.
THOMAS D. ALLEN—2. Ophthalmic surgery.
I. MUSKAT—2. Clinical and surgical otolaryngology; plastic surgery of face and nose.

COLUMBUS HOSPITAL

Monday

MICHAEL GOLDENBURG—2. Emergency surgery of the eye.

Wednesday

G. B. LAMBRAKIS—9. Indications for operative treatment in acute mastoiditis.
S. SCIARETTA—9. Otolaryngological clinic.
MICHAEL GOLDENBURG—2. Eye surgery.

Friday

MICHAEL GOLDENBURG—2. Eye surgery.

ST. LUKE'S HOSPITAL

Monday

EARL VERNON—1. Ophthalmological clinic.

Tuesday

E. FINDLAY and RICHARD GAMBLE—1. Ophthalmological clinic.

J. T. CAMPBELL, JOHN A. CAVANAUGH, HORACE R. LYONS, E. P. NORCROSS and WALTER H. THEOBALD—2. Otolaryngological clinic.

Wednesday

ALVA SOWERS—1. Ophthalmological clinic.

J. T. CAMPBELL, JOHN A. CAVANAUGH, HORACE R. LYONS, E. P. NORCROSS and WALTER H. THEOBALD—2. Otolaryngological clinic.

Thursday

FRANK BRAWLEY and JAMES W. CLARK—1. Ophthalmological clinic.

J. T. CAMPBELL, JOHN A. CAVANAUGH, HORACE R. LYONS, E. P. NORCROSS and WALTER H. THEOBALD—2. Otolaryngological clinic.

Friday

E. FINDLAY and RICHARD GAMBLE—1. Ophthalmological clinic.

JOHN B. MURPHY HOSPITAL

Monday

E. F. GARRAGHAN—2. Eye operations.

Tuesday

L. H. WOLF and PAUL WOLF—10. Mastoid surgery.

Friday

GEORGE W. MAHONEY—9. Cataracts.

CHILDREN'S MEMORIAL HOSPITAL

Wednesday

GEORGE S. LIVINGSTON and staff—9. Otolaryngological clinic.

RICHARD C. GAMBLE and staff—2. Ophthalmological clinic.

WASHINGTON BOULEVARD HOSPITAL

Tuesday

L. MCBRIDE—2. Nose and throat clinic.

Wednesday

VIRGIL WESCOTT—2. Eye clinic.

ILLINOIS CENTRAL HOSPITAL

Tuesday

HIRAM SMITH—9. Eye clinic.

Wednesday

JAMES H. MCLAUGHLIN—9. Nose and throat surgery.

GRANT HOSPITAL

Wednesday

S. H. SOBOROFF—9. Ear, nose and throat clinic.

GEORGE F. SUKER—9. Eye clinic.

GEORGE DENNIS—9. Eye, ear, nose and throat clinic.

MOUNT SINAI HOSPITAL

Monday

JOSEPH C. BECK, ALFRED LEWY, NOAH SCHOOLMAN, JACOB LIFSCHUTZ, S. M. MORWITZ and associates—2. Ear, nose and throat operations.

Friday

JOSEPH C. BECK, ALFRED LEWY, JACOB LIFSCHUTZ, NOAH SCHOOLMAN, S. M. MORWITZ and associates—9. Ear, nose and throat operations.

JAMES E. LEBENSOHN—9. Operations for cataract and squint.

Daily, 9 and 2

JAMES E. LEBENSOHN. Eye changes in hypertensive states.

ALFRED LEWY and S. M. MORWITZ. Otogenic sepsis.

OAK PARK HOSPITAL

Tuesday

HOWARD RIORDAN—9. Demonstration of new nasopharyngoscope on the cadaver and living.

Thursday

HOWARD RIORDAN—9. Treatment of maxillary sinusitis with the cold quartz lamp; new method of treatment of maxillary polypi by diathermy.

Friday

GEORGIANA THEOBALD—9. Demonstration of eye tumors; ophthalmic surgery.

CHICAGO MEMORIAL HOSPITAL

Monday

RICHARD H. STREET and RICHARD W. WATKINS—2. Otolaryngological clinic.

Tuesday

HERMAN P. DAVIDSON and GLENWAY W. NETHERCUT—9. Eye clinic.

Wednesday

ALFRED E. LEWY and IRVING I. MUSKAT—2. Otolaryngological clinic.

WEST SUBURBAN HOSPITAL

Monday

ROBERT H. GOOD—2. Surgery of the nose, motion picture demonstration.

Tuesday

JOHN J. THEOBALD—2. Mastoid surgery.

Wednesday

GEORGIANA THEOBALD—2. Eye pathological exhibit.

AMERICAN HOSPITAL

Tuesday

HARRY L. POLLOCK AND ASSOCIATES—2. Ear, nose and throat clinic.

Wednesday

OSCAR KRAFT—2. Ophthalmological clinic.

AUGUSTANA HOSPITAL

Wednesday

ALFRED MURRAY—2. Eye, ear, nose and throat clinic.

WOMEN AND CHILDREN'S HOSPITAL

Tuesday

ALICE K. HALL—10. Nose and throat clinic.

Wednesday

FRANCES HAINES—10. Nose and throat clinic.

PASSAVANT MEMORIAL HOSPITAL

Friday

J. GORDON WILSON, JOHN DELPH, CARL BOOKWALTER and ELLISON ROSS—9. Ear, nose and throat clinic.

SANFORD GIFFORD, WILLIAM MANN, JR. and RALPH DAVIS—11. Ophthalmology.

ILLINOIS MASONIC HOSPITAL

Tuesday

M. H. COTTLE—10. Some advances in mastoid work.

B. M. WOLIN—10. Tonsil surgery in the poor risk cases.

H. E. TAYLOR—10. Conservative surgery of the nose.

EVANGELICAL HOSPITAL

G. HENRY MUNDT. Technique and interpretation of hearing tests and technique and interpretation of tests of the static labyrinth.

ST. BERNARD'S HOSPITAL

Friday

PHILIP O'CONNOR—2. Surgery of the eye, dry clinic.

LITTLE COMPANY OF MARY HOSPITAL

Wednesday

H. T. NASH—10. Emergency surgery of the eye.

SOUTH SHORE HOSPITAL

Monday

JOHN W. STANTON—2. Mastoiditis and its complications.

Thursday

JOHN W. STANTON—11. Otolaryngological surgery.

ST. ANNE'S HOSPITAL

Tuesday

B. T. GORDON—9. Nose and throat clinic.

Wednesday

W. K. GRAY—9. Eye and ear clinic.

ST. MARY OF NAZARETH HOSPITAL

Tuesday

J. J. KILLEEN—9. Ear, nose and throat clinic.

Thursday

J. J. KILLEEN—9. Ear, nose and throat clinic.

SOUTH CHICAGO COMMUNITY HOSPITAL

Tuesday

GEORGE E. PARK—3. The center of ocular rotation in the horizontal plane.

JACKSON PARK HOSPITAL

Tuesday

H. E. L. TIMM—1. Timm's modification of Sluder tonsillectomy.

FRANCES E. WILLARD HOSPITAL

Thursday

WILLARD D. BRODE—10. Surgery of throat and nose.